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CONTENTS OF VOLUME IX

JANUARY, 1915. NUMBER 1

PAGE

Summary of Four Years of Clinical and Bacteriologic Experience with Meningitis in New York City. Phebe L. DuBois, M.D., and Josephine B. Neal, M.D., New York 1

The Lange Gold Chlorid Reaction on the Cerebrospinal Fluid of Infants and Young Children. C. G. Grulee, M.D., and A. M. Moody, M.D., Chicago 17

Acidosis with Auto-Intoxication in Infants and Children: A Study of One Hundred Consecutive Cases in Apparent Epidemic Form. Carleton R. Metcalf, M.D., Concord, N. H. 29

A Respiration Incubator for the Study of the Energy Metabolism of Infants. John R. Murlin, Ph.D., New York 43

Intravenous Injection of Diphtheria Antitoxin in Children. Edwin Henry Schorer, M.D., Kansas City, Mo. 59

The Sugar-Content of the Blood in Childhood. Murray H. Bass, M.D., New York 63

A Pocket Baby Scale. C. R. Spicer, M.D., Chicago 70

Progress in Pediatrics: Review of Progress in Ophthalmology. Howard F. Hansell, M.D., Philadelphia 72

Current Pediatric Literature 76

FEBRUARY, 1915. NUMBER 2

PAGE

The Energy Metabolism of Ten Hospital Children, between the Ages of Two Months and One Year. John R. Murlin, Ph.D., New York, and B. Raymond Hoobler, M.D., Detroit 81

Whey in Infant-Feeding. Studies of Infant-Feeding: Fifth Paper. A. W. Bosworth, Geneva, N. Y., H. I. Bowditch, Boston, and B. H. Ragle, Boston 120

Treponema Pallidum Found at Autopsy, in the Blood-Stream and Elsewhere, in a Case of Congenital Syphilis. H. C. Clark, M.D., and I. N. Gates, M.D., Ancon, C. Z. 126

The Voice Sign in Chorea — Technic of Elicitation. Studies in Neurologic Technic No. 3. Walter B. Swift, M.D., Boston 132

Book Reviews: Säuglingsernährung und Säuglingsstoffwechsel. Von Leo Langstein und Ludwig F. Meyer 134

Progress in Pediatrics: Résumé of Work on Tuberculosis in Children for 1914. May Michael, M.D., Chicago 135

Current Pediatric Literature 181

American Journal of Diseases of Children

VOL. 9 MARCH, 1915 No. 3

THE SCHICK TOXIN REACTION FOR IMMUNITY IN DIPHTHERIA *

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As is well known, immunity in diphtheria is generally incomplete and of short duration. Even an attack of this disease with consequent stimulation of the body cells with diphtheria toxin and the formation of homologous antitoxin and other antibodies does not confer for any considerable length of time that immunity which is so characteristic of scarlet fever, measles and small-pox. Passive immunization with antitoxin confers an immunity even more fleeting, because the immune serum constituents are quickly eliminated or destroyed. For this reason, Smith, Park, and more recently von Behring have suggested an active form of immunization in diphtheria by means of toxin-antitoxin mixtures, as the antitoxin prepared by our own body cells is more lasting. In order to estimate the degree of immunity following injections of these toxin-antitoxin (T-A) mixtures, it is necessary to determine the amount of antitoxin per cubic centimeter of serum in units or fractions of a unit. For this purpose Römer's intracutaneous technic with the guinea-pig has been used, but the method is rather too uncertain and complicated for the routine examination of large numbers of persons.

Schick[1] has proposed a very simple clinical test for this purpose; it is based on the observations of von Behring that as little as one-hundredth of a unit of antitoxin per cubic centimeter of our serum will protect a person against diphtheria. Schick has determined that when an amount of diphtheria toxin equal to one-fiftieth the *minimal lethal dose* (M. L. D.) for a guinea-pig weighing from 250 to 300 gm. is injected intracutaneously in the human skin, if one-thirtieth or more antitoxin per cubic centimeter of serum is present this dose of toxin is neutralized and no reaction follows; if less than this amount of antitoxin is present or none at all, the toxin injected remains unneutralized and produces a local inflammatory reaction of erythema and edematous

* Received for publication Jan. 22, 1915.
* From the Laboratory of the Philadelphia Hospital for Contagious Diseases.
1. Schick: Munchen. med. Wchnschr., 1913, lx, 2608.

infiltration. This toxin test may be used for determining the response to active immunization by means of the T-A mixtures; it does not, however, serve the purpose of a quantitative estimation of antitoxin in the body fluids, but is simply a ready clinical index based on the observation that, when properly performed, a negative test may be regarded as indicating that a state of immunity more or less satisfactory exists, whereas a positive reaction indicates the absence of antitoxin and a state of susceptibility to diphtheria.

It has also found a very useful and practical application in testing persons for natural diphtheria antitoxin, especially those who have been exposed to the infection. The logical conclusion would be that only those who react positively are susceptible to diphtheria and require passive immunization by means of an injection of antitoxin.

In this country the Schick test has been used quite extensively by Park, Serota and Zingher,[2] who report favorably on its practical value. We have been interested in this test during the past year, having made 1,265 inoculations, and are likewise able to subscribe to the value of the test, especially for the purpose of detecting those persons susceptible to diphtheria, on the basis that their blood contains no natural antitoxin or too small an amount for adequate protection.

The objects of this study were as follows:

1. To apply the toxin skin test to a large number of apparently normal persons to determine susceptibility to diphtheria at different ages.

2. To determine quantitatively the antitoxin content of the blood-serum of persons reacting positively, slightly positively, doubtfully and negatively in order to study further the toxin test under conditions in which the quantity of antitoxin in the blood is known.

3. To study the degree and duration of immunity to diphtheria in normal persons following an injection of diphtheria antitoxin.

4. To study the degree and duration of immunity among persons suffering with scarlet fever and receiving an injection of diphtheria antitoxin.

5. To study the degree of immunity during and following an attack of diphtheria.

6. To study the practical value of the toxin skin test in determining which persons should be immunized with antitoxin when exposed to diphtheria.

TECHNIC OF THE SCHICK TEST

Preparation of the Toxin.—It is advisable to prepare the toxin for this test from a strong diphtheria toxin in order to reduce by high

2. Park, W. H., Serota, M. H., and Zingher, A.: Arch. Pediat., 1914, xxxi, 481; Active Immunization in Diphtheria and Treatment by Toxin-Antitoxin, Jour. Am. Med. Assn., Sept. 5, 1914, p. 859.

dilution the amount of protein constituents of the bouillon medium to a minimum. The *minimal lethal dose* (M. L. D.) of a toxin is first determined by injecting varying amounts of the diluted toxin subcutaneously in a series of guinea-pigs weighing between 250 and 300 gm. The least amount of toxin killing a pig at the end of four days is the minimal lethal dose. For the test Schick uses one-fiftieth this amount of toxin so diluted that it is contained in 0.1 c.c.; Park uses the same amount diluted in 0.2 c.c.

After trying both methods we have adopted one-fortieth this amount of toxin as our dose and dilute it with sterile normal salt solution containing 0.25 per cent. phenol in such manner that it is contained in 0.05 c.c. With this technic we have produced less trauma and have fewer doubtful reactions.

Only ripened toxins should be titrated and used because the toxin deteriorates rapidly under ordinary circumstances. We usually dilute the L + dose of toxin[3] 1 : 100, determine the minimal lethal dose and from this make up the 1 : 40 dilution for the Schick test. It is necessary to retitrate and make up fresh dilutions for the Schick test every two or three weeks and the toxin should always be kept at a low temperature to retard deterioration as much as possible.

Method of Injection.—The injection is made intracutaneously by pinching up a fold of skin between the index-finger and thumb and inserting the needle into the epidermis. As the injection is made a whitish spot develops and a slight stinging pain is felt; if this raised anemic area is not seen the injection is probably too deep and unsatisfactory.

A very fine needle (No. 26) and a perfectly adjusted syringe are necessary. We have used with much satisfaction the Record and Fournier's tuberculin syringes. Platinum iridium needles are especially useful, as they are readily sterilized in a flame and are thus adapted for giving a large series of injections.

Injections are readily given in the skin of the arm near the insertion of the deltoid muscle after cleansing with alcohol and drying the skin.

The Reaction.—This appears in from twenty-four to forty-eight hours after injection and is charactertized by an area of erythema with a brownish tinge measuring from 0.5 to 2 cm. in diameter and accompanied by slight edematous infiltration of the underlying tissues (see accompanying plate). In colored persons the erythema can usually be seen, although not always sufficiently well to measure, but the edema is readily palpable. The reaction usually reaches its height in

3. We wish to express our thanks to Dr. A. Parker Hitchens for much of the L + toxin used in this study.

from forty-eight to seventy-two hours and then begins to fade within a week or ten days, accompanied by some itchiness and usually followed by a brownish pigmented area of some days' or weeks' duration. A slight superficial scaling, due to the necrosing effect of the toxin on the superficial epithelial cells is generally noticed. In the majority of instances there is no general reaction.

Occasionally, the reaction is so slight that the observer is in doubt whether to regard it as purely traumatic or a weakly positive result. For this reason we make the total amount injected 0.05 c.c. in order to reduce trauma to a minimum. We have regarded any reaction measuring more than 3 to 5 mm. in diameter as positive; a very faint areola with no palpable infiltration about the needle hole was regarded as probably traumatic and negligible.

Park and his associates have observed in a small proportion of cases what they term pseudoreactions characterized by earlier development, more infiltration and less sharply circumscribed lesions disappearing in from twenty-four to forty-eight hours leaving a faintly pigmented spot which does not scale. These reactions are regarded as local anaphylactic reactions due to protein contained in the bouillon medium. We have regarded all reactions except those evidently traumatic as positive; the extent of the reaction is modified by the presence of varying amounts of natural antitoxin in the blood of the patient.

It is to be remembered that the true toxin reaction is purely irritant and inflammatory, and due to the direct action of the toxin on the local cells; it is not an anaphylactic reaction due to the action of a protein split product (proteotoxin) or anaphylatoxin.

Cutaneous Method.—We have also conducted this test by abrading the skin of the forearm in two places by means of a von Pirquet scarifier. A drop of toxin (L + dose = 0.82 c.c.) was then applied to the lower of the two scarifications and gently rubbed into the tissues for a few seconds.

At the end of from twenty-four to forty-eight hours a small area of erythema could be readily seen about the inoculation site in most persons who showed a positive intracutaneous reaction. In colored children the edema could usually be appreciated by mere inspection or palpation.

We used the two methods of inoculation simultaneously in a large number of persons, but prefer the intracutaneous method, as by the cutaneous test the results are more difficult of interpretation and the inoculation more painful to the patient.

THE TOXIN REACTION IN PERSONS OF VARIOUS AGES

The toxin test was applied in 447 persons, most of whom were apparently healthy and well; a few were suffering with various chronic

diseases and were tested while undergoing observation and treatment in the wards of various hospitals in Philadelphia.

The results are summarized in Table 1.

The reaction has demonstrated that children between the ages of 1 and 8 years are most susceptible to diphtheria. It also shows that a small percentage of children under 1 year of age are likewise susceptible to this infection and supports the well-known clinical observation that while most cases of diphtheria occur among children from 1 to 5 years of age the disease is unfortunately by no means rare among infants.

TABLE 1.—THE TOXIN SKIN REACTION IN PERSONS OF VARIOUS AGES

Age, Years	Total Tested	Reactions		Per Cent. Positive
		Positive	Negative	
Under 1	25	3	22	12
1-2	21	9	12	43
2-4	18	12	6	66
4-6	12	7	5	58
6-8	14	8	6	57
8-15	21	5	16	24
15-30	142	60	82	42
Over 30	194	55	139	28
Total	447	159	288	41

TABLE 2.—PERCENTAGE OF PERSONS OF VARIOUS AGES SUSCEPTIBLE TO DIPHTHERIA *

Age, Years	Percentage of Positive Toxin Reactions			Incidence of (14,000 cases)
	Park	Kolmer	Schick	
Under 1	40	12	7	3.2
1-5	65.9	54.5	53	45.4
5-10	42.5	57.8	50	32.2
10-15	26	24	50	8.1
Over 15	33	35	10	11.4

* According to the toxin reaction and an analysis of 14,000 cases of diphtheria in the Philadelphia Hospital for Contagious Diseases.

The percentage of susceptible persons of various ages as shown by the toxin test is higher than statistics in diphtheria indicate; at least this is apparently true in Philadelphia (Table 2). Likewise the percentage of positive reactions observed by Schick, Park and ourselves, while in general about parallel, are somewhat discrepant, especially

among children from 1 to 5 years of age. We believe Dr. Park's figures are mainly based on observations among children suffering with scarlet fever, and this probably explains his higher percentage of positive reactions, for as we shall point out later, scarlet fever reduces resistance to diphtheria as indicated both by clinical data and a higher percentage of positive toxin reactions among persons with this disease.

It is but natural to expect the toxin reaction to show a higher percentage of susceptible persons than would be indicated by statistics in diphtheria, for many factors modify the infectiousness of the disease, as virulence of the bacillus, crowding, etc., and only under exceptional circumstances would one expect all susceptible persons exposed to diphtheria to contract the disease.

Cultures were made of the throats of a large number of persons tested, but there was no relation between the presence or absence of diphtheria bacilli and the toxin reaction. Natural antitoxic immunity cannot be ascribed to the presence of bacilli in the upper air-passages at least, with consequent stimulation of body cells and formation of antitoxin; at present there is apparently no satisfactory explanation to account for the production of natural antitoxin in some persons and its absence in others.

THE ANTITOXIN CONTENT OF THE SERUM OF PERSONS REACTING POSITIVELY AND NEGATIVELY TO THE TOXIN TEST

According to Schick, persons reacting positively to the toxin test usually contain less than one-thirtieth of a unit of antitoxin per cubic centimeter of serum. Park and his associates agree with this conclusion.

We have titrated the antitoxin content of the serums of a number of persons reacting negatively, weakly positively and strongly positively to the toxin test and give the results of some of these in Tables 3, 4 and 5. In some instances the results were indefinite and these have been omitted.

Technic.—For the purpose of measuring small amounts of antitoxin as fractions of a unit, Römer's intracutaneous method is generally employed.

We conduct this test as follows: An L + toxin is diluted 1 : 10 or 1 : 100, and from this stock dilution further dilutions are prepared with sterile normal salt solution. In a series of small sterile test-tubes are placed 0.2 c.c. of these varying dilutions of toxin and to these are added 0.2 c.c. of a solution of carefully standardized antitoxin each 0.1 c.c. of which contains $\frac{1}{1000}$ unit. The cotton stoppers of these tubes are paraffined to prevent evaporation, the contents of each tube are mixed by gentle shaking and all tubes incubated for an hour or two and then stood aside in a refrigerator over night.

Next morning 0.2 c.c. of each tube is injected intracutaneously in a guinea-pig (site prepared by pulling out the hairs). From three to five injections are made into the abdominal skin of one pig. The amount injected contains 0.1 c.c. of the toxin and 0.1 c.c. antitoxin ($\frac{1}{1000}$ unit); the balance is allowed for waste. The pigs are observed for three or four days and the toxin, which just produces roughening of the skin, is taken as the "limes-necrosis" (L_n) dose.

This determination having been made, varying amounts of the person's serum are mixed with this constant quantity of toxin and the tests conducted as described. If, for example, 0.002 c.c. of a patient's serum mixed with the L_n dose of toxin gave the same amount of necrosis in the same time as the identical quantity of the toxin with $\frac{1}{1000}$ standard unit, then 1 c.c. of this person's serum contains 0.5 unit.

TABLE 3.—Antitoxin Content of the Serums of Persons Reacting Negatively to the Toxin Test

No.	Name	Age, Years	Antitoxin in Units per Cubic Centimeter of Serum
1	Dr. K.	24	10 units.
2	Dr. R.	36	10 units.
3	L. F.	24	About 1 unit.
4	M. L.	½	About 10 units.
5	W. P.	1½	About 10 units.
6	J. S.	3	About 1/10 unit.
7	P. B.	8	About 4 units.
8	I. L.	3½	From about 1/30 to 1/20 unit.
9	B. N.	4	From 1/10 to 1 unit.
10	S. F.	12	About 10 units.
11	M. G.	7	1 unit.
12	M. I.	3	About 6 units.
13	W. B.	5	About 2 units.
14	J. C.	20	From 1/20 to 1/10 unit.
15	B. M.	6	1/20 unit.
16	P. A.	4	1/20 unit.
17	C. H.	7	From 1/10 to 1 unit.
18	F. H.	2	From 1 to 2 units.
19	M. A.	1½	About 1/10 unit.
20	B. B.	8	About 1 unit.

We have obtained much better results, however, with the technic used by Park and Zingher.[4] This consists in diluting a toxin so that 1 c.c. contains one-fortieth the L+ dose. By mixing 0.2 c.c. of patient's serum with 0.2 c.c. of toxin, allowing to stand at room temperature for thirty minutes and injecting 0.1 c.c. of the mixture intracutaneously in the abdominal surface of a guinea-pig (prepared by pulling out the hairs) we are testing for one-fortieth unit of antitoxin to each cubic

4. Personal communication.

centimeter of serum. By using twice the quantity of serum we may test for one-eightieth unit and by so varying the quantities of serum and toxin in this manner the method is well adapted for determining quantities of antitoxin varying from 10 units to $\frac{1}{320}$ unit.

TABLE 4.—ANTITOXIN CONTENT OF THE SERUMS OF PERSONS REACTING WEAKLY POSITIVE TO THE TOXIN TEST

No.	Name	Age, Years	Toxin Reaction Erythema in cm.	Antitoxin in Units per Cubic Centimeter of Serum
1	H. F.	36	0.5 × 0.7	From 1/40 to 1/20 unit.
2	Dr. M.	24	0.3 × 0.5	About 1/80 unit.
3	E. F.	30	0.6 × 0.4	1/40 unit.
4	E. S.	3	0.5 × 0.5	1/40 to 1/80 unit.
5	—. G.	25	0.5 × 0.5	1/20 to 1/10 unit.
6	C. S.	10	0.4 × 0.7	1/80 to 1/40 unit.
7	A. M.	5	0.3 × 0.6	1/60 unit.
8	F. C.	16	0.5 × 0.5	About 1/20 unit.
9	J. L.	20	0.6 × 0.6	About 1/40 unit.
10	M. P.	4	0.3 × 0.5	1/80 to 1/40 unit.
11	A. S.	11	0.6 × 1.0	1/10 unit.
12	A. M.	8	0.5 × 0.8	1/80 to 1/40 unit.

TABLE 5.—ANTITOXIN CONTENT OF THE SERUMS OF PERSONS REACTING STRONGLY POSITIVE TO THE TOXIN TEST

No.	Name	Age, Years	Toxin Reaction Erythema in cm.	Antitoxin in Units per Cubic Centimeter of Serum
1	—. B.	21	1 × 1.5	About 1/40 unit.
2	—. U.	23	1 × 1.2	1/40 to 1/20 unit.
3	Dr. K.	28	1.5 × 2.0	None.
4	Dr. M.	27	1.8 × 2.0	About 1/60 unit.
5	A. B.	8	2.0 × 2.5	None.
6	M. T.	7	3.0 × 3.2	None.
7	M. W.	4	1.0 × 1.5	1/60 to 1/88 unit.
8	K. W.	6	2.0 × 2.8	None.
9	C. B.	4	1.0 × 1.8	About 1/60 unit.
10	K. B.	2½	1.5 × 1.8	1/80 to 1/40 unit.

We generally make from two to four inoculations in each pig at the same time; thus with the serum of a person reacting negatively we may test for $\frac{1}{20}$ and $\frac{1}{10}$, or 1 and 2 units simultaneously.

The pigs are observed for three or four days when the results are recorded. Distinct roughening of the skin with superficial necrosis is regarded as positive and indicating incomplete neutralization. The injection of serum alone may leave a small nodule, but the skin over

The Schick test for immunity in diphtheria. Dr. J. A. K., a well-marked reaction thirty-six hours after the intracutaneous injection of one-fortieth the minimum lethal dose of a diphtheria toxin diluted to 0.05 c.c. The patient's blood contained no antitoxin. The brownish erythematous area with edematous infiltration of the subcutaneous tissues are characteristic of the reaction.

Illustrating Article by John A. Kolmer, M.D., and Emily L. Moshage, M.D.
American Journal of Diseases of Children, March, 1915.

it is smooth. Park and Zingher advise heating fresh serums to 55 C. for half an hour before testing in order to prevent or reduce this knob-like lesion. We have not found this generally necessary.

An examination of these tables shows the following:

1. The serums of persons reacting negatively to the toxin test usually contain at least $\frac{1}{20}$ unit of antitoxin per cubic centimeter of serum. In one instance about $\frac{1}{30}$ unit was found. This agrees quite closely with the results of Schick and Park, who found that $\frac{1}{30}$ unit was usually sufficient to neutralize the toxin. Probably the slight difference in our results is due to the fact that we use one-fortieth instead of one-fiftieth of the minimum lethal dose as the amount of toxin injected.

2. It is interesting to note that the serums of 5 per cent. of persons tested contained at least 10 units of antitoxin per cubic centimeter of serum. It may be that the antitoxin content of some of these was still higher, but our titrations were not continued beyond this determination.

3. The serums of persons reacting weakly positive to the toxin test usually contained from $\frac{1}{40}$ to $\frac{1}{160}$ unit of antitoxin per cubic centimeter. In one instance as much as $\frac{1}{10}$ unit was found and in several others about $\frac{1}{20}$ unit.

4. The serums of persons reacting strongly positive were found to contain less than $\frac{1}{20}$ unit per cubic centimeter of serum and frequently none at all could be detected.

THE DURATION OF PASSIVE IMMUNITY TO DIPHTHERIA AS STUDIED BY THE TOXIN SKIN TEST

Clinical experience with diphtheria antitoxin as an immunizing agent has long since taught that sufficient passive immunity to insure adequate protection does not usually persist over three or four weeks, and not infrequently is of much shorter duration. For this reason efforts are being made to perfect a method of active immunization with toxin-antitoxin mixtures, because the antitoxin produced by our own body cells persists in the body fluids for longer periods of time.

We have applied the toxin test to 108 children varying in age from 2 months to 3 years, all of whom had received 1,250 units of antitoxin by subcutaneous injection at varying intervals of time prior to the tests. The results are shown in Table 6. Most of these children were feeding cases or convalescents and only a few were suffering with an acute infection as broncho-pneumonia.

Among children from 2 months to 3 years of age a positive toxin reaction could be expected in about 40 per cent. It is of interest to note that the immunity conferred by 1,250 units of antitoxin, equal

approximately to 100 to 400 units per kilo of body weight, was apparently efficient for ten days; after this interval antitoxin rapidly disappeared, so that after four to six weeks the immunity may be regarded as having entirely disappeared.

TABLE 6.—THE TOXIN SKIN REACTION IN CHILDREN WHO HAD RECEIVED 1,250 UNITS OF ANTITOXIN

Days After Injection of Antitoxin	Total	Toxin Skin Reaction		Per Cent. Positive
		Positive	Negative	
1-5	10	0	10	0
5-10	18	0	18	0
10-20	12	3	9	25.0
20-30	14	4	10	28.5
30-50	36	13	23	36.1
Over 7 weeks	16	7	9	43.7
Total	106	27	79	

TABLE 7.—THE TOXIN SKIN REACTION IN SCARLET FEVER PATIENTS WHO HAD RECEIVED 2,500 UNITS OF ANTITOXIN BY SUBCUTANEOUS INJECTION

Days After Antitoxin	Total	Toxin Skin Reaction		Per Cent. Positive
		Positive	Negative	
1-5	60	2	58	3.3
5-10	45	3	42	6.6
10-20	65	9	56	13.9
20-30	77	17	60	22.0
30-40	50	17	33	34.0
40-50	37	21	16	56.7
Over 50	28	19	9	67.8
Total	362	88	274	

THE DURATION OF PASSIVE IMMUNITY TO DIPHTHERIA AMONG PERSONS SUFFERING WITH SCARLET FEVER AS STUDIED BY THE TOXIN SKIN TEST

As is well known, persons suffering with scarlet fever are rendered peculiarly susceptible to diphtheria, especially from the third to the sixth week of the disease. Cases of postscarlatinal diphtheria are much more common in hospital than in private practice, as it occasionally happens that in a large hospital ward cases of secondary diphtheria remain undetected and expose other patients to the infection. Further than this, it would appear that during the early stages

of scarlet fever natural immunity to diphtheria is reduced as it is to streptococcus infection.

We have applied the toxin skin test to 362 persons in the various stages of scarlet fever and at varying intervals of time following the subcutaneous injection of 2,500 units of antitoxin. As the antitoxin is administered as a routine measure within from twelve to twenty-four hours after admission to the hospital, the stage of the disease may be estimated in the table according to the number of days after the injection of serum. With the exception of a few adults, all of these patients were from 2½ to 14 years of age.

When compared with Table 6 it will be found that in *scarlet fever passive immunity following the injection of diphtheria antitoxin is of shorter duration than that induced among approximately normal children, in that 10 per cent. of the former are susceptible within ten days after receiving antitoxin.* Whether this is due to accelerated elimination of the horse-serum antitoxin during the acute stages of scarlet fever or to other causes we are unable to state.

This increased susceptibility to diphtheria among scarlet fever patients is also shown in Table 8, compiled from the results of toxin tests among children of the same age.

TABLE 8.—PERCENTAGE OF POSITIVE TOXIN REACTIONS AMONG NORMAL CHILDREN AND CHILDREN WITH SCARLET FEVER *

	Days		
	1-10	10-20	20-60
Percentage of positive reactions in normal children after 1,250 units of antitoxin.....	0	25	36
Percentage of positive reactions in children with scarlet fever after 2,500 units antitoxin.....	3	20	36

* Children aged 1 to 8 years.

Cultures of the throat were made in all of these cases, but there was no relation between the percentage of carriers and positive toxin reaction. Thus 46 of these persons showed the presence of diphtheria bacilli mostly of the solid types; of these, 10 gave a positive and 36 a negative toxin reaction.

A STUDY OF IMMUNITY DURING AND FOLLOWING AN ATTACK OF DIPHTHERIA BY MEANS OF THE TOXIN SKIN TEST

We have applied the toxin skin test to 350 persons, mostly children, suffering with diphtheria and receiving antitoxin treatment. This study was of much interest for two reasons:

1. From the possibility of throwing some light on the question of dosage of antitoxin.

2. To determine the degree of immunity induced as a result of active stimulation of body cells by the diphtheria toxin of the patient's infection.

All these patients were being treated in the diphtheria department of the Philadelphia Hospital for Contagious Diseases. Antitoxin was given in doses varying from 10,000 to 100,000 units, the average being 45,000 units, by subcutaneous injection. The patients were mostly children from 2 to 15 years of age. As a general rule, the first dose of antitoxin was given during the first forty-eight hours of the infection. The results of the toxin skin tests are summarized in Table 9.

TABLE 9.—THE TOXIN SKIN REACTION AMONG PERSONS SUFFERING WITH DIPHTHERIA AND RECEIVING ANTITOXIN

Days After Antitoxin	Total	Toxin Skin Reaction		Per Cent. Positive
		Positive	Negative	
1-5	81	14	67	17.2
5-10	86	22	64	25.5
10-20	96	33	63	34.3
20-30	40	14	26	35.0
30-50	28	13	15	46.4
Over 50	19	13	6	68.4
Total	350	109	241	

As shown in this table, a rather large proportion of patients reacted positively, especially within the first ten days of the disease and after receiving antitoxin. Among children of the ages of these patients a positive toxin reaction could be expected in from 40 to 50 per cent. As shown in the tables, these patients were in general just as susceptible after an attack of diphtheria as before; in other words, it would appear that the body cells produced little or no homologous antitoxin and the immune antitoxin is soon eliminated. This has an important bearing on the use of T-A mixtures in active immunization and indicates that antitoxic immunity is acquired only with prolonged stimulation of the body cells.

As stated, the high percentage of positive reactions during the first ten days of the disease and after large doses of antitoxin was quite surprising. As a general rule, these occurred among children with severe infections. We have listed a few of these in Table 10.

It is difficult to find an explanation for the relatively high percentage of positive reactions so soon after large doses of antitoxin. Naturally, one may suppose that the immune antitoxin is quickly neutralized so that the toxin injected intracutaneously is not neutralized. This supposition receives some support in view of the observation that most, not all, of the positive skin reactions occurred among those

with severe infections, as if heavy toxin production at the site of infection neutralized the large amount of antitoxin administered. If this is true, the claim that large doses of antitoxin are required in the treatment of diphtheria receives support.

TABLE 10.—THE TOXIN SKIN REACTION AMONG PERSONS SUFFERING WITH DIPHTHERIA AND RECEIVING ANTITOXIN

No.	Age, Years	Diagnosis	Antitoxin Units	Days After Antitoxin	Positive Toxin Reaction (cm.)
54	2	Tonsillar diphtheria.	23,000	3	2 × 1.5
55	10	Tonsillar diphtheria.	20,000	4	1 × 0.5
107	7	Tonsil. and Laryn. diph.	50,000	6	0.3 × 0.4
3	5	Tonsil. and Laryn. diph.	50,000	8	1 × 1.0
61	10	Tonsillar diphtheria.	60,000	8	2 × 2.0
65	15	Tonsil. and Laryn. diph.	175,000	8	2 × 2.5
69	6	Tonsillar diphtheria.	40,000	8	1 × 0.6
87	15	Tonsil. and Laryn. diph.	75,000	6	1 × 1.2
100	3	Tonsil. and Laryn. diph.	45,000	8	0.4 × 0.5
106	5	Tonsil. and Laryn. diph.	30,000	9	0.6 × 0.5
68	7	Tonsillar diphtheria.	30,000	11	1.5 × 1.5
16	13	Tonsil. and Laryn. diph.	60,000	13	0.5 × 0.6
43	8	Tonsillar diphtheria.	40,000	13	1 × 1.2
23	5	Tonsillar diphtheria.	23,000	15	1 × 1.0
6	8	Tonsil. and Laryn. diph.	50,000	18	1 × 1.2
1	5	Tonsil. and Laryn. diph.	35,000	19	1 × 1.0
30	3	Tonsillar diphtheria.	30,000	19	1 × 1.0
36	2	Tonsil. and Laryn. diph.	30,000	17	0.5 × 0.6
18	9	Tonsil. and Laryn. diph.	45,000	16	1.5 × 2.0
44	7½	Tonsillar diphtheria.	45,000	13	1 × 1.2

PRACTICAL VALUE OF THE TOXIN SKIN REACTION

On the assumption that a negative toxin reaction indicates that an individual possesses sufficient immunity to diphtheria to afford protection in case of exposure, the chief practical value and application of this test would be for the purpose of detecting non-immune individuals and immunizing these only instead of all persons indiscriminately. This not only would prove of importance from the point of view of economy, but also would spare many persons the discomfort of an injection of serum and consequent sensitization by horse protein.

We have had one experience that has greatly increased our confidence in the practical value of this toxin reaction. During the past year a nurse in the Polyclinic Hospital contracted diphtheria and was sent for treatment to the Philadelphia Hospital for Contagious Diseases. Within forty-eight hours the toxin skin test was applied to all nurses as well as resident physicians, patients and attendants in the Polyclinic Hospital. All nurses reacting positively were given 2,500 units of antitoxin by subcutaneous injection. Those reacting negatively were not immunized.

Within two weeks five nurses contracted diphtheria and all of these were among those who had shown a positive skin test and had received antitoxin. None of those persons reacting negatively to the skin test contracted the disease. The first nurse sent to the hospital to aid in nursing contracted diphtheria; unfortunately a toxin test had not been made in her case. A second nurse who reacted negatively was sent to the hospital to aid in the care of the infected nurses; she did not receive a prophylactic injection of antitoxin and did not contract the disease. Later one of the nurses reacting negatively to the toxin test complained of sore throat and inspection showed redness of the fauces and a few spots of exudate on one tonsil; a series of cultures showed the presence of streptococci and staphylococci, but no diphtheria bacilli. In a few days the patient was again on duty.

One of the patients who reacted negatively showed diphtheria bacilli in the throat which were virulent for guinea-pigs; for this reason the patient was removed to the hospital under the assumption that he may be a dangerous carrier. There were absolutely no clinical evidences of diphtheria.

While we must wait several years during which the reaction may be tried under similar circumstances before a final verdict of its practical value may be expressed, we believe that this test will prove quite reliable as a guide in determining which persons should be immunized under conditions of exposure. This is especially true in institutions as hospitals, asylums and the like. The test also finds ready application in private practice and since additional evidence at hand indicates that a person reacting negatively tends to react similarly for an indefinite period, physicians may test children at intervals to determine the state of their resistance to diphtheria.

In the presence of an outbreak of diphtheria therefore, the physician should take cultures and apply the toxin test to all persons exposed. At the end of twenty-four hours he has the evidence offered by both at hand. *This delay of twenty-four hours before immunizing with antitoxin is justifiable unless a contact shows clinical signs suggestive of diphtheria. In such an instance we believe that antitoxin should be given at once.*

The reaction has a special field of usefulness in hospitals and wards for the care of children. All children should be subjected to the toxin test prior to admission and those immunized who react positively. If it is the custom to reinject with antitoxin a month or six weeks later it is better practice to apply the toxin test first and administer serum to those only who show a positive reaction. This means a saving of antitoxin and the avoidance of disagreeable serum sickness.

The toxin test will probably not prove of value in handling the difficult problem of the diphtheria carrier. Our experiences with this class of cases may be summarized as follows:

A. Persons may harbor in the upper air-passages diphtheria bacilli virulent for guinea-pigs and react negatively to the toxin test. Presumably the absence of both symptoms and reaction are due to the presence of antitoxin in the blood serum. One such person had about 5 units of antitoxin per cubic centimeter of his serum. While such persons may be in apparent good health, nevertheless they constitute a danger to others.

B. Several diphtheria convalescents harboring bacilli virulent for guinea-pigs reacted positively to the skin test, but showed no clinical evidences of diphtheritic intoxication.

C. In a number of instances bacilli that proved non-virulent for guinea-pigs have been isolated from the throats, noses and ears of persons reacting positively to the toxin test. As already stated, we have found no relation between the toxin reaction and the percentage of diphtheria bacilli carriers; in the majority of such instances it is probable that the bacilli are harmless. Park and his associates have employed the test in scarlet fever patients, and while more than one-fourth of those reacting negatively became carriers no cases of clinical diphtheria developed among them.

Apparently, there is but one reliable means of determining the disease-producing powers of a given culture of diphtheria bacilli, namely, the guinea-pig inoculation test. *In the absence of clinical signs and symptoms the toxin reaction offers no aid in this direction.* In persons *showing some clinical evidences of an infection, particularly a dirty nasal discharge containing diphtheria-like bacilli, or a tonsillitis showing staphylococci or streptococci and a diphtheria bacillus, we are inclined to agree with Park that the toxin test may possess some diagnostic value.* If the person reacts negatively, diphtheria may be excluded on the basis that antitoxin in the blood-serum sufficient to effect neutralization of the test toxin will protect the individual against diphtheria; on the other hand, a positive reaction indicates that diphtheria is still a probability on the basis that the individual is shown to be at least susceptible to the infection.

It is to be remembered that a person reacting positively will not necessarily contract diphtheria even though exposed. Of twenty-five nurses and attendants in the scarlet fever department of the hospital, no less than sixteen reacted positively; many of these have been exposed to diphtheria many times during a period of several years and have received no antitoxin and nevertheless have escaped infection.

SUMMARY

1. The toxin skin reaction is a valuable and reliable method for detecting susceptibility to diphtheria.

2. Persons reacting negatively to this test usually contain at least $\frac{1}{20}$ unit of diphtheria antitoxin per cubic centimeter of serum, and this amount of antitoxin is probably sufficient to protect against infection.

3. Persons reacting weakly or strongly positive usually contain less than $\frac{1}{40}$ of a unit of antitoxin per cubic centimeter of serum or none at all. These persons may be regarded as susceptible to diphtheria and in the event of exposure to infection should be passively immunized with an injection of antitoxin.

4. About 40 to 50 per cent. of children ranging from 1 to 15 years of age react positively to the toxin test; this means that the preliminary use of the toxin test will eliminate the necessity of administering prophylactic doses of antitoxin to about 50 per cent. of children.

5. The toxin reaction indicates that the immunity conferred by an injection of antitoxin begins to disappear after ten days and has generally passed away entirely after four weeks.

6. The increased susceptibility of persons with scarlet fever to diphtheria is shown by the toxin reaction; even after the injection of antitoxin about 10 per cent. are susceptible within ten days.

7. According to the toxin reaction the immunity conferred by an attack of diphtheria is usually of short duration or entirely absent.

8. The most practical application of the toxin reaction consists in applying the test as a preliminary measure to all persons who have been exposed to diphtheria and immunizing only those who react positively.

We wish to express our thanks to Dr. S. McC. Hamill, Dr. J. P. C. Griffith, Dr. W. Hollopeter, Dr. A. Eshner and other physicians for the clinical opportunities afforded us in various Philadelphia hospitals.

Second and Luzerne Streets.

BLUE SCLEROTICS ASSOCIATED WITH BRITTLE BONES

REPORT OF A CASE IN A CHILD TWO YEARS OLD *

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WITH COMMENT BY DR. PERCY H. FRIDENBERG
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Blue-tinged sclerotics are not infrequently seen in infants and young children. In tuberculous patients also such a blue tinge may occasionally be noted. Congenital heart disease with marked cyanosis may be associated with blue sclerotics, and is largely due to venous congestion. In negro infants and children I have sometimes noted patches of pigmentation in the sclerotics. The blue sclerotics which I am about to describe are entirely distinct from any of these. The condition is congenital and the sclerotics are of a uniform blue color. The first to note the peculiarity was von Ammon;[1] his description is as follows:

> Congenital diseases of the sclerotic are rare. . . . Of importance is a peculiar whitish blue coloration of this membrane occasionally met with when the whole development of the eye is retarded. The sclerotic in such cases appears thin and almost transparent. I have seen it also in congenital hydrophthalmus. . . . A similar thinness occurs in patients suffering from congenital heart disease. In that case the sclerotic is dark blue, this being due partly to the thin condition of the membrane and partly to an accumulation of venous blood and a large mass of pigment in the eye.

In 1903 Buchanan[2] made the first microscopic examination and found:

> The cornea and sclerotic were unusually thin, the cornea being three-fifths and the sclerotic one-third of its normal thickness. Histological examination showed that the fibers of the cornea and sclerotic were of about normal size, but unusually few in number. The anterior elastic lamina was entirely absent.

The hereditary transmission of blue sclerotics was first pointed out by Peters[3] in 1908. He reported cases occurring in four generations. Four of his patients also showed a typical embryontoxon.[4]

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* Received for publication Jan. 1, 1915.
* Read before the Section on Ophthalmology, the New York Academy of Medicine, Jan. 18, 1915.

1. Von Ammon: Darstellungen der Krankheiten und Bildungsfehler des menschlichen Auges, 1841, iii, 73.
2. Buchanan: Tr. Ophthal. Soc. U. Kingdom, 1903, xxiii, 267.
3. Peters: Klin. Monatsbl. f. Augenh., 1908, p. 130; Die angeborenen Fehler und Erkrankungen des Auges, 1909, p. 80.
4. An extension of the upper layers of the sclerotic into the cornea. Pressure of the lids is said to cause accentuation at the upper and lower corneosclerotic margin.

Peters also regarded the condition as due to an abnormally thin or abnormally transparent sclerotic. In 1910 Stephenson[5] described a series of twenty-one cases occurring in four generations of one family. In two cases the presence of an arcus senilis or an embryontoxon was noted. Subsequent investigation enabled Harman[6] to add another generation to this family, so that of a total of fifty-five members, thirty-one showed the same congenital peculiarity with some slight individual differences. By referring to Figure 1, it will be seen that the condition is transmitted only through affected members; it never skips a generation, and no members with white sclerotics transmit blue sclerotics to their offspring. About 50 per cent. of the children born to parents with blue sclerotics show the anomaly.

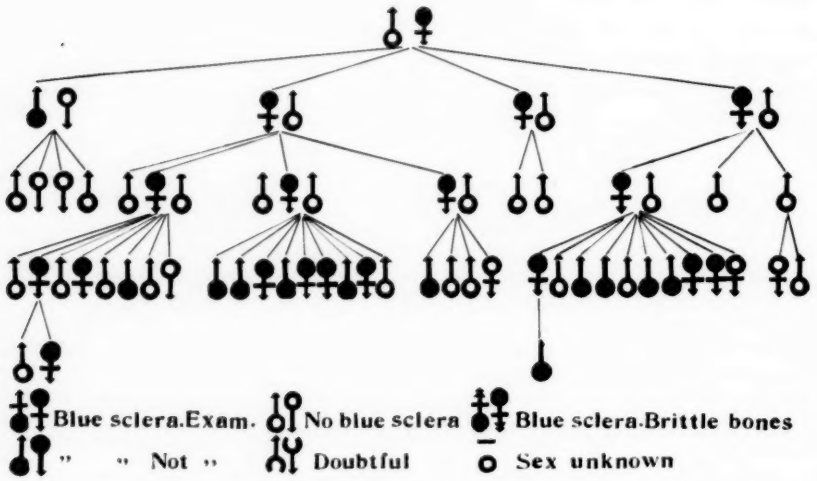

Fig. 1.—Chart of Stephenson and Harman's series of cases of blue sclerotics.

The first author to mention the association of blue sclerotics with brittle bones was Eddowes.[7] In 1900 he published a brief report on "Dark Sclerotics and Fragilitas Ossium," in which he described a case in a young woman whose father also had a similar condition. He mentions having seen some years previously a boy with blue sclerotics who in the course of two years during which he was under observation had nine fractures.

In 1911 Burrows[8] reported a series of cases occurring in four generations of one family, in which, of twenty-nine individuals,

5. Stephenson: Ophthalmoscope, 1910, viii, 330.
6. Harman: Ophthalmoscope, 1910, viii, 559.
7. Eddowes: Brit. Med. Jour., 1900, ii, 202.
8. Burrows: Brit. Med. Jour., 1911, ii, 16.

thirteen had blue sclerotics and nine of those fractures also (Fig. 2). Of these nine, seven had multiple fractures.

In 1912 Adair-Dighton[9] published a report of four generations of blue sclerotics; of thirty-two individuals, twenty-one had blue sclerotics (Fig. 3), and several of these brittle bones. During the last two years cases have also been reported by Conlon,[10] Cockayne[11] and Ostheimer.[12] Rolleston's[13] case, which was associated with congenital syphilis, probably belongs to this group.

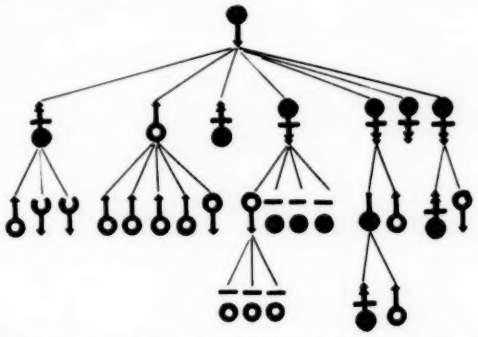

Fig. 2—Chart of Burrows' series of cases of blue sclerotics associated with fragility of bones.

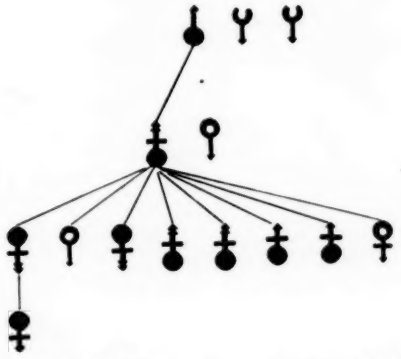

Fig. 3.—Chart of Adair-Dighton's series of cases of blue sclerotics associated with fragility of bones.

REPORT OF CASE

The following is a brief account of a boy of 2 years whom I have recently observed:

The patient was first seen in February, 1914, at the age of 20 months. The parents are apparently healthy, but the father is rather small and thin, weighing only 120 pounds; the mother is of average size and robust. As far as the

9. Adair-Dighton: Ophthalmoscope, 1912, x, 188.
10. Conlon: Boston Med. and Surg. Jour., 1913, clxix, 16.
11. Cockayne: Ophthalmoscope, 1914, xii, 271.
12. Ostheimer, Maurice: Fragelitas Ossium, Jour. Am. Med. Assn., Dec. 5, 1914, p. 1996.
13. Rolleston: Brit. Jour. Child. Dis., 1911, p. 202.

parents know, no other members of the family have had blue sclerotics or brittle bones. There were no miscarriages; no evidence of syphilis or other constitutional disease. The parents have been married eleven years and have three children besides the patient. Two of these children I have examined and found perfectly normal. They began to walk and talk at the proper age. The patient was born normally and nursed for ten months. The first teeth appeared at 8 months, and the child began to sit up at 9 months. At 20 months (February, 1914) he was not yet able to stand or to talk distinctly. In December, 1913, he fell from an ordinary chair and fractured his right tibia, and six weeks later while in bed with the cast still applied, he sustained a fracture of the right femur. He began to walk at 23 months and now at 2½ years can say

Fig. 4.—E. G., aged 30 months; blue sclerotics associated with brittle bones.

short sentences. Physical examination on Dec. 16, 1914, aged 30 months, shows (Fig. 4) a small, thin, fair-haired boy distinctly below the normal, both physically and mentally. Height 32 inches (81 cm.), weight 22 pounds.

	Patient	Normal
Head—Biparietal, diameter	14 cm.	13.5 cm.
Above the ears, diameter	13 cm.	12 cm.
Occipitofrontal, diameter	17 cm.	17 cm.
Circumference of head	51 cm.	48.5 cm.
Circumference of chest	48 cm.	49.7 cm.
Circumference of abdomen	47 cm.	

The head is large and brow prominent, the fontanel closed. The sclerotics are of a distinct peculiar blue color throughout. The patient has sixteen teeth. There are no signs of rickets, no rosary, no enlargement of the epiphyses. The examination of the chest is negative. There is no congenital heart dis-

ease. Radiographic examinations of the legs and arms were made. In the patient I employed a method which I have used for a number of years. The extremity of the patient was taken with that of a normal child of the same age at the same time on the same plate. In this way even those not accustomed

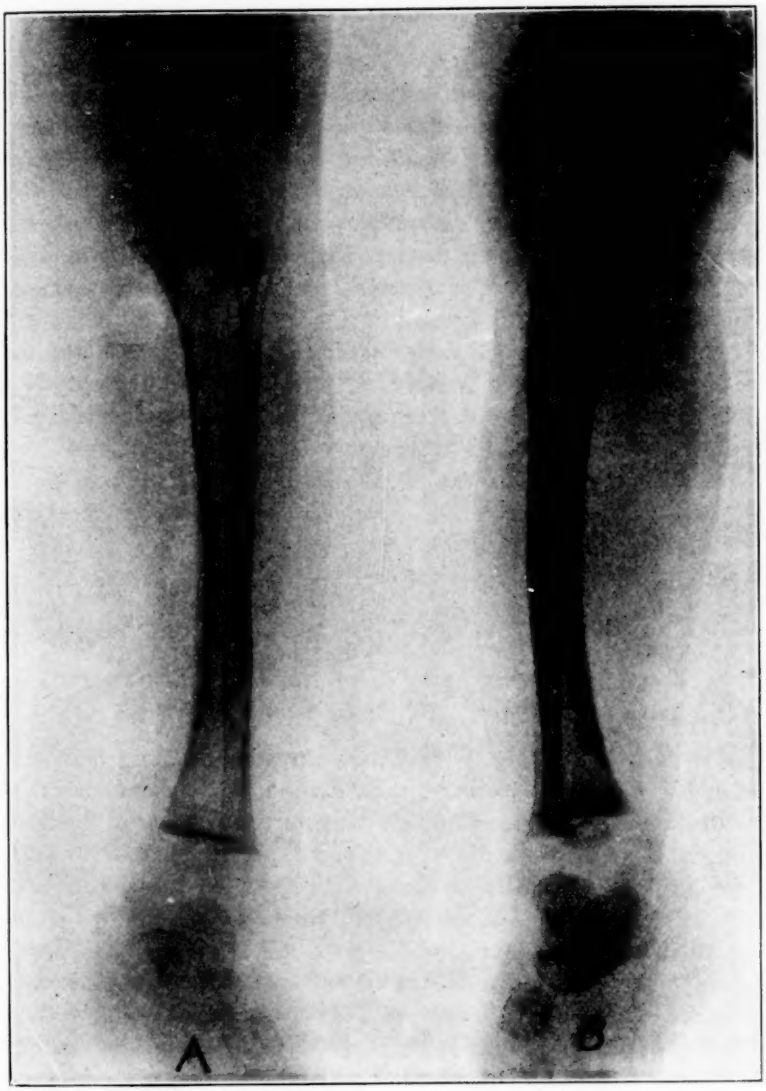

Fig. 5.—Right femur and tibia (*A*) of E. G., aged 18 months; taken on same plate at same time of femur and tibia (*B*) of normal infant of 18 months.

to interpret plates will have no difficulty in detecting differences in structure. It will be seen (Fig. 5) that all trace of the fracture has disappeared. Comparing the two bones, it will be noted that in length and thickness they are about the same, but one is far more transparent and lacks density. It is deli-

cate in structure especially towards the proximal end of the tibia; hardly any cortical portion is seen; the epiphyseal ends are broadened and show a distinct lack of cortical substance. Not only the bones but also the soft parts, the muscles and ligaments show the same lack of density, which indicates a diminished amount of fibrous tissue. The roentgenogram of the arm, in striking contrast to that of the leg, shows very little change from the normal (Fig. 6).

The patients affected with this combination of blue sclerotics and brittle bones are usually small and delicate, frequently fair-haired. The large size of the head is mentioned in several cases. Whether the intelligence is slightly retarded in many cases I cannot say. In my own patient his inability to run and play with other children may have had something to do with the matter. In another patient whom I saw through the courtesy of Dr. Reitzfeld, a boy of fifteen years, the intelligence was apparently normal.

The color of the sclerotic varies in different individuals from a pale azure or porcelain blue to a leaden hue. The color is uniform throughout and involves the entire sclerotic from the cornea as far as the eye

Fig. 6.—Hand and arm of E. G., aged 30 months.

ball is visible. According to Rolleston, the color is more distinct on some days. Usually there is no accentuation in the ciliary zone, but Harman mentions one case in which the color was deeper in the ciliary region and masked toward the equator on account of the increased thickness of the overlying conjunctiva, and also masked in those regions in which the muscle tendons overlay the globe. As was pointed out by Buchanan and others, the fibrous tissue is abnormally thin; the individual fibers are of normal thickness, but are deficient in number. The cornea is thin and the anterior elastic lamina is absent, which is said to account for the astigmatism frequently present in these patients. The choroid is also abnormally thin, which causes Fuchs' coloboma and the oval appearance of the optic disks (Stephenson, Harman). As to the bones, there seems to be a defect in the quality and quantity of fibrous tissue forming the framework which causes a lack of elasticity and the tendency to fracture. This change is well shown in the radiographs, and, as has been pointed out, not only the bones, but also the soft parts are also affected so that sprains are not infrequent. I

have no doubt that a careful examination will reveal changes in structure and a lack of fibrous tissue in other parts of the body. The change in the eye is so apparent that it would naturally be the first part noticed. According to Ostheimer,[12] of thirty-two patients with "fragilitas ossium" who were able to go about, only six were noted to have blue sclerotics, but I have no doubt that in a few other cases the peculiar color of the eye may have been overlooked. Not all patients who have blue sclerotics have brittle bones, but in the families in which blue sclerotics was an inherited peculiarity, all those members who had brittle bones had blue sclerotics also. The blue sclerotics like the fragility of the bones, may, however, occur independently of hereditary transmission. Ostheimer[12] states that in only eight of 117 cases of "fragilitas ossium" was the condition known to exist in either parent and in only twenty-four was it present in brothers or sisters.

COMMENT BY DR. FRIDENBERG

Ophthalmologic examination of the little boy with blue sclerotics shows no abnormality of the eyes beyond just this peculiar condition. The color of the sclerae is uniform, as far back as it can be seen. I should call it a Delft or china blue, as it has a decidedly grayish cast. I also notice a peculiar leaden-gray color of the iris, like that seen in the newly-born, and think this may be of significance. I am not aware that it has been noted by previous observers in these cases, and will refer to its causation later on. The vision seems acute, and there is but slight ametropia. The child was very restless, and I could, at best, make out a general hyperopic refraction. The fundus was not deeply pigmented, in contrast to the case examined by Stephenson. In fact, I should call it very blond if not suggesting, at least, albinism. The disks were perfectly normal in appearance and of the usual size and shape. I might mention here that the congenital crescent downward or Fuchs' coloboma was seen in but one of these cases, and is occasionally noted in otherwise perfectly normal eyes. I do not think it has any significance for us.

As to these blue sclerotics, it was early recognized that they are due, not to any actual pigmentation, but to the unusually translucent sclera allowing the brown-black choroid to shine through, as it were, producing a color interference. That a thinning is the principal cause of this optical condition is, I think, disproved by the fact that there was in all these cases, say more than fifty, no mention of sclerectasia or of a distention of the globe in the form of infantile glaucoma or hydrophthalmos, and no ophthalmoscopic evidence in any case, of a giving way at the posterior pole (coloboma, posterior staphyloma). The condition quoted from Ammon is, as indicated in the title, some-

thing quite different, namely, a case of true infantile glaucoma or hydrophthalmus with marked thinning of the sclera, and consequent bluish translucency.

To come back to the peculiar lead-gray iris in this case, the normal color of this membrane ordinarily depends on color interference, the brown-black of the posterior or pigment layer shining through more or less as the pigment in the stroma is absent, scanty or marked. Where the pigment is entirely absent we get a light gray-blue iris which is translucent, the pink or rabbit eye of albinism. The marked transparency of both sclera and iris, in spite of an apparently normal or but slightly reduced thickness, is, I believe, due merely to absence of lime salts in the connective tissue elements of these structures. Lime salts are the deposits which as we know produce opacities in the ocular media which appear white to reflected light. Transillumination did not show any remarkable difference from the normal eye, and this again, I think, indicates that there is at least no excessive thinning of the sclera. I doubt, too, very much, whether there is in most or in any of these cases an actual absence of the anterior elastic lamina or of any other layer of the cornea, as such a condition occurring in early life would, I am sure, give rise not only to astigmatism, but to marked keratoglobus or conical cornea if not to even more decided developmental anomalies.[14]

The following passage in Dr. Herrman's paper is significant: "Not only the bones but the soft parts, the muscles and ligaments show the same lack of density, which indicates a deficient amount of fibrous tissue." If we lay stress on the defective quality, that is, lack of lime salts, of actual calcification and ossification, rather than on the amount of fibrous tissue, I think we shall be more nearly right. This is indicated by the roentgenograms of the fragile bones, which were found to be of about normal length and thickness. It is probable, as this passage suggests, that all connective tissue throughout the body is lacking in density, and it would be interesting to examine, among other structures, the nails, teeth and hair for further evidence of this anomaly.

250 West Eighty-Eighth Street.

14. The correctness, or rather, the applicability of Buchanan's findings have been questioned (see Conlon).

THE CHEMICAL COMPOSITION OF DIARRHEAL AS COMPARED WITH NORMAL STOOLS IN INFANTS*

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It has been a matter of considerable surprise on going through medical literature to see how little has been written regarding the chemical composition of diarrheal as compared with normal stools. Stools of all varieties have been studied in many ways in great detail since the work of Uffelmann and Wegscheider about forty-five years ago. Numerous reports have been published of metabolism work which contain stool analyses made with reference to the different constituents, fat, nitrogen, ash, etc.; and scattered through these are found reports of isolated instances in which very loose stools have been studied, but, so far as we are aware, no attempt has been made to correlate the observations on diarrheal stools and compare them with those which were normal. The work done on diarrheal stools as such has been chiefly a study of the flora.

It was with the belief that some new light might possibly be thrown on the treatment of such conditions, dietetic and otherwise, that we have made from another point of view a restudy of our metabolism observations, namely, to determine the actual chemical composition of diarrheal stools and compare them with the normal.

Those whose observation on infants' stools is limited to an inspection of napkins can form but an imperfect idea of even the gross condition of the infants' excretions, especially as to the amount of water which they contain. When stools are received in a metabolism basin a very different impression is made.

With the two large factors in the production of loose stools, that is, increased secretion and increased peristalsis, every one is familiar. But many questions arise relating to diarrheal stools. Do very loose stools differ from normal ones only in that they contain more water, or do they actually represent a much greater loss of solids? Are all the solids in the stool affected to the same degree, or are some drained

* Submitted for publication Nov. 15, 1914.
* Read at a meeting of the American Pediatric Society, Stockbridge, Mass., May 26, 1914.
* From the Laboratories of the Babies' Hospital and the Rockefeller Institute.

away much more than others? Does the actual loss, or the percentage of intake lost, vary only with the food, or are there other important factors?

These were some of the questions regarding which it was thought information might be gained by such a study as that undertaken. The data have been derived by going through the records of our metabolism studies for the past four years and selecting from them the cases illustrating the different types of stools. Such records were especially valuable for our purpose, for, although the children studied differed considerably with respect to their condition and the food given, the exact intake of the different food elements had been determined, as well as the composition of the excretion. In a few of the early cases the stool analysis did not go further in the ash estimation than to determine the total ash; but in all the recent ones, including the greater number studied, the composition of the ash had been fully worked out.

While the chemical composition of the stools was much influenced by the food, it did not seem to make much difference what the exciting cause of the diarrhea happened to be, as its effect in draining away fluids and solids from the body was much the same in all cases studied.

For the purpose of this study the cases were divided into (A) formed, firm or pasty stools; (B) loose stools and (C) very loose stools. The division into loose and very loose is a somewhat arbitrary one. We classed as "loose" those in which the total quantity of water lost varied between 100 and 200 c.c. daily; as "very loose" those in which the water exceeded 200 c.c. daily.

No account was taken of the number of evacuations during the day, first, because in metabolism observations this is somewhat difficult to determine, and secondly, for the reason that it is really of little importance. What is essential is the total daily excretion.

In the group A, of stools of normal consistency and appearance, there were observations made on 9 patients for 11 periods. In the group B, loose stools, there were observations made on 8 patients for 14 periods. In the group C, very loose stools, observations were made on 6 patients for 10 periods. In all, observations were made on 21 patients for 35 periods, for a total of 128 days.

A different period signifies an observation on the same child at another time or on another food. In all but two instances each period was for a longer time than a single day; usually it was three or four days. This was found convenient and sometimes necessary, since in estimating some of the salts of the ash, of which the quantity was very small, the total secretion of two or three days was needed for a satis-

factory quantitative determination. The amounts of the substances given in the table represents an average for the period. Two or three days were put in the same period only when the food was the same and the stools similar in character. In all cases daily averages of all the observations are given in the charts, and in several cases we have given the range. The extreme variations were considerable, but not greater than one would expect and not enough to affect the general significance of the findings.

The type of child studied is indicated in the clinical summary of cases appended (Table 1).

The average age of the twenty-one children was 9 months (the range being from 4 to 13 months) and the average weight 5,500 gm. (about 12½ pounds). In general, they would be classed as hospital nutrition cases. Those in Group A, however, were digesting well and gaining satisfactorily in weight; those in Groups B and C were suffering from acute, or more often subacute diarrhea, usually of a non-febrile character. There were no dysenteric cases and none of acute infection or intoxication of the intestines of a severe type.

It will be seen from the table that most of the infants were taking formulas derived from whole milk by various dilutions. This was true in twenty of the thirty-five periods studied. The exact percentages of the milk formulas are given in the table. The numerals indicate the fat, sugar and protein, given in order. Thus, in Case 1, Group A, the food was fat, 2.4 per cent.; sugar, 5 per cent.; protein, 1.8 per cent. The sugar added was lactose unless otherwise specified. In sixteen periods some preparation of maltose was given. Usually this was a fluid preparation, a mixture of maltose and dextrin.

The protein milk (*Eiweissmilch*), which was the food in five periods, was made from whole milk and had the following average composition: Of seven samples, fat 3.00; sugar 2.90; protein 4.00; ash 0.70. It was prepared in 10-quart quantities by precipitating 4 per cent. milk with rennet; the curd was carefully washed twice with water and then rubbed through a fine wire sieve with the addition of 10 pints of special buttermilk (fat-free lactic acid milk) and water added up to 10 quarts.

The high ash content of protein milk shown by the analyses was to us a surprise, since the impression has prevailed that the salts have been much reduced by the removal of the whey and by the washing of the curd. These results, however, were based on seven complete examinations including thirteen samples, some of these being composite samples. Prepared in the manner described, the range of the salts in protein milk was from 0.54 to 0.74 per cent.

TABLE 1.—Clinical Summary of the Cases Studied

GROUP A (STOOLS OF NORMAL CONSISTENCY)

No.	Name	Age, Months	Weight, Gm.	Food	Period	Duration, Days	No. Stools a Day	Gross Appearance
1	P. L.	10	9,600	2.4; 5; 2.2. With barley flour	1	3	1-2	Brownish-yellow, largely formed, smooth, firm.
1	P. L.	10	9,600	Same as preceding.....	2	3	1-2	Like preceding.
2	D. W.	5	5,800	1.8; 5; 1.6	1	3	4	Dry, pasty, yellow-brown, not homogeneous.
2	D. W.	5	5,800	Same as preceding.....	2	3	2	Like preceding.
3	W. H.	12	7,000	2; 5; 1.8. With cereal gruel	1	3	3	Pasty, gray-green, mostly smooth, partly formed.
3	W. H.	12	7,100	Same as preceding.....	2	3	2	Mostly smooth, formed, gray, some softer, greenish.
4	F. H.	11	4,500	¾ protein milk; ¼ barley water	1	4	3-4	Mostly formed, soft, yellow-gray, smooth.
5	J. S.	7½	4,100	1.45; 4.5; 4. Made like protein milk	1	3	1-5	Mostly formed, yellow-gray, smooth.
6	A. R.	8	5,445	Protein milk with barley flour	1	3	3	Formed, dry, constipated.
6	A. R.	8½	5,695	2.4; 2.6; 2.2. With barley flour	2	3	1-2	Similar, but not so hard.
7	F. B.	4	5,745	Protein milk and rice flour	1	3	2-4	Pasty, smooth, largely formed, brownish yellow.
				GROUP B (LOOSE)				
1	D. W.	5	5,700	1.8; 5; 1.6. With malt.....	1	4	5	Watery, greenish, curds and sour.
2	J. D.	5	3,900	1.6; 2; 1.4. With cane sugar and barley flour	1	4	5	Partly thin, pasty; partly watery, granular, greenish.
3	V. C.	4	4,400	1.8; 2.2; 2. With barley flour	1	3	8	Watery, fine fat curds, sour, greenish-yellow color.
4	E. R.	10	7,500	1.8; 5; 2. With cereal.....	1	3	4-5	Watery, yellow, fat curds, mucus.
4	E. R.	10	7,400	Same as preceding.....	2	3	5	Partly watery, partly solid, green, sour, mucus.
4	E. R.*	10½	7,300	1; 5; 2. With cereal gruel..	3	4	3-4	Watery, partly green, large curds and mucus, sour.

5	B. S.	12	8,200	2; 5; 1.8. With cereal gruel	1	4	3	Watery, gray-green, granular, foul.
6	W. H.	13½	6,700	2.6; 5; 2.4. With cereal gruel	1	3	4	Watery, yellow, fat curds and mucus.
7	F. H.	11	4,800	0; 4.5; 3.5. With cane-sugar	1	3	11 13	Orange-yellow, pasty, watery, and much mucus and hard curds.
7	F. H.	11	4,700	1.6; 4.7; 3. With cane-sugar	2	3	8-10	Watery and pasty, smooth, curds and mucus.
7	F. H.	12	5,200	2; 4.5; 2.6. With dextrimaltose and sodium phosphate	3	4	5-10	Watery, foamy, fat and hard curds and mucus.
8	J. G.	7½	4,400	2.4; 5; 2.2.....	1	4	4-5	Watery, fat and hard curds, large fragments.
8	J. G.	8	4,500	Same, plus 6 dr. maltose	2	3	4-6	Watery and soft, spongy, small curds.
8	J. G.	8	4,600	Same, plus 9 dr. maltose	3	3	3	Watery, brownish-yellow, hard curds, foul.

GROUP C (VERY LOOSE)

1	B. S.	12	7,700	2; 5; 1.8. With cereal.....	1	2	5-8	Very watery, green, with fat curds and mucus.
2	V. C.	4	4,700	1.8; 5; 2. With barley flour	1	4	6	Watery, green, with large fat curds; sour.
2	V. C.	4	4,500	1.8; 2.2; 2. With barley flour	2	5	7	Like preceding with mucus also.
3	C. B.	8	4,900	2.6; 5; 2.4. Olive oil 1½ dr.; changed to protein milk	1	5	5	At first pasty with fat curds, then green, very watery, with fat and hard curds and mucus.
4	F. H.	10	4,500	2.6; 5; 2.4	1	8	11	Watery, green, foamy, fat curds and mucus.
4	F. H.	10	4,600	2.6; 5; 2.4.....	2	9	9	Very watery, green, large fat curds. and mucus.
5	W. S.	5	4,600	1.6; 5; 1.4.....	1	2	6	Watery, greenish, little solid matter.
5	W. S.	5	4,600	Same as preceding, with 8 to 12 c.c. of malted milk	2	8	4-7	Watery, greenish, little solid matter.
5	W. S.	5	4,400	Fat-free milk and soy-bean gruel	3	1	7	Watery, greenish, little solid matter.
6	D. L.	9	5,200	1.8; 5; 2.1.....	1	1	10	Watery, green, with curds and mucus; sour.

Table 2 gives the percentage of water and dried matter in stools of different types, showing both the averages and the range met with in the series.

TABLE 2.—PERCENTAGE COMPOSITION OF STOOLS STUDIED

	Stools of Normal Consistency		Loose		Very Loose	
	Seven Patients Eleven Periods		Eight Patients Fourteen Periods		Six Patients Ten Periods	
	Average %	Range %	Average %	Range %	Average %	Range %
Water	80.3	(73-85)	91	(88-92)	93	(90-96)
Dried matter..	19.7	(15-27)	9	(8-12)	7	(4-10)

METHODS EMPLOYED

Food and feces were each dried on a steam-bath to a constant weight in equilibrium with room temperature and humidity, and all the determinations were made on this dried material. Each of the urine values was obtained separately from liquid samples. The fat in both the food and the feces was determined by extracting with ether according to a modification of the Soxhlet method and weighing the extract.

Total nitrogen was determined in the dried material and in the urine by the Kjeldahl-Gunning method. We have in our tables regarded all the nitrogen as representing protein; with the knowledge, however, that there is here a small error, as other nitrogen compounds, not protein, are present both in the urine and the stools and possibly also in the food. The amount, however, is so small in the infant as to be negligible for our purposes.

Total ash in dried food and feces and in urine evaporated to dryness was determined in most cases by the Stolte method. According to this method a platinum dish containing the sample is set on pieces of broken pipe-clay inside a porcelain dish. Low heat from a large-sized Teklu burner is applied to the porcelain dish until the material is well charred, after which the heat is gradually increased to the greatest possible point. When most of the black has disappeared the platinum dish is covered by a piece of platinum foil and the heating continued until ashing is completed. No sodium or potassium chlorid is volatilized by this treatment. A few of the earlier samples here reported were ashed over a free flame with the addition of a few drops of acid.

Chlorin was determined in the urine by titration with silver nitrate, according to Volhard. In the dried material in most of the samples the extract, to which nitric acid and ferric alum had been added, was filtered after several hours' standing and titrated with silver nitrate. In the earlier cases the sample was charred, sometimes after being mixed with sodium carbonate, extracted with water, filtered and the filtrate was titrated with silver nitrate.

Phosphates in the urine were determined by titration with uranium acetate or nitrate, potassium ferrocyanid being used as indicator. In the dried material the Neumann method has been used in most cases, that is phosphoric acid precipitated in the ashed material as phosphomolybdate, dissolved by ammonia and reprecipitated by magnesia mixture as magnesium ammonium phosphate and weighed after ignition as pyrophosphate. In some of the earlier samples the Vozárik method was followed. According to this the material is well mixed with magnesium oxid and ashed, the residue dissolved in hydrochloric acid, sodium acetate and acetic acid added to the neutralized solution and phos-

TABLE 3.—Total Daily Excretion

	Stools of Normal Consistency			Loose			Very Loose		
	Seven Patients Eleven Periods			Eight Patients Fourteen Periods			Six Patients Ten Periods		
	Average		Range	Average		Range	Average		Range
Water (c.c.)	35.6	.....	(18. -50.)	133.	.....	(107. -195.)	293.	.....	(217. -555.)
Dried matter (gm.)	8.75	.....	(6. -13.1)	12.95	.....	(10.43 - 16.76)	21.16	.....	(12.6 - 37.35)
Fat (total)	3.12	.....	(0.91 - 7.07)	4.04	.....	(0.43[1] - 7.35[2])	7.97	.....	(1.39[3]- 12.95)
Neutral fat	.....	1.09	(0.38 - 2.08)	.....	2.83	(0.43[1] - 6.48[2])	.....	5.70	(1.37[3]- 8.24)
Free-fatty acids	.....	0.34	(0. - 2.04)	.....	0.72	(0.[4] - 1.44)	.....	2.44	(0. - 7.29)
Soap fats	.....	1.69	(0.46 - 5.40[5])	.....	0.50	(0.[6] - 1.91)	.....	0.74	(0.[7] - 2.17)
Protein	2.26	.....	(1.31 - 3.19)	3.56	.....	(2.42 - 5.76)	5.56	.....	(3.80 - 10.7)
Ash (total)	2.17	.....	(1.21 - 3.58)	2.72	.....	(1.47 - 5.93[8])	3.96	.....	(3.03 - 4.78)
CaO	.....	1.02	(0.46 - 1.70)	.....	1.08	(0.42 - 2.33)	.....	0.83	(0.70 - 0.96)
MgO	.....	0.096	(0.03 - 0.164)	.....	0.10	(0.025 - 0.15)	.....	0.12	(0.10 - 0.16)
P_2O_5	.....	0.63	(0.14 - 1.28)	.....	0.70	(0.12 - 1.53)	.....	0.59	(0.49 - 0.68)
Cl	.....	0.022	(0.008- 0.032)	.....	0.14	(0.05 - 0.37)	.....	0.28	(0.27 - 0.30)
K_2O	.....	0.180	(0.084- 0.300)	.....	0.36	(0.22 - 0.52)	.....	0.82	(0.68 - 0.97)
Na_2O	.....	0.041	(0. - 0.256)	.....	0.17	(0.11 - 0.31)	.....	0.36	(0.19 - 0.67)

1. Infant on fat-free milk.
2. Infant on milk containing 1-8 per cent. fat.
3. Infant on fat-free milk.
4. Two infants had none.
5. Very large stools, normal; infant gaining.
6. Six infants had none.
7. Two infants had none.
8. Fat-free milk; intake 9.86.

phoric acid determined by titration with uranium nitrate. Calcium and magnesium, sodium and potassium were determined in dried material of food and feces and urine by the ordinary methods, calcium being precipitated as oxalate and weighed as oxid, magnesium weighed as pyrophosphate, sodium and potassium separated as chlorids and potassium determined by precipitation with platinic chlorid.

Tables 3 and 4 give the actual and the percentage composition of the stools of different types. Very loose stools contain not only a very large amount of water, but the quantity of dried matter lost daily is much greater than that lost in stools of normal consistency. It varies somewhat with the food, but principally with the amount of water.

Fat.—The fats particularly vary in most cases directly with the amount of water. A child who is losing twice as much water is usually losing twice as much fat in his stool. A very high fat loss, however, is also sometimes seen in dry, formed, soapy stools. The average loss of fat in loose stools was two and a half times that seen in normal stools. The percentage of fat varies widely; the average was 37.7 per cent. of the dried matter in the very loose stools, the highest found being 62.2 per cent. of the dried matter of the stool. The highest found in stools of normal consistency was 54 per cent.

The form of fat differs much in the different types of stools. In the normal pasty stools the soap fats are present in largest amount. The soaps form on the average 54.3 per cent., while the neutral fat forms but 39.4 per cent. of the total fat of the stool. In very loose stools these ratios are reversed. The greatest proportion of the fat (64.2 per cent.) is neutral fat, while soaps form but a small proportion (8.3 per cent.) of the total. In eight observations on infants with loose or very loose stools, no soaps at all were formed. This is what might be expected to occur when the intestinal contents are hurried through the bowel too rapidly for saponification to take place. Free fatty acids represent those not combined with bases to form soaps; their amounts also were higher in the loose than in the normal stools and much higher in the very loose stools.

Protein.—The daily amount of protein lost in the stools calculated from the nitrogen is about two and a half times greater in very loose than in normal stools; it being in about the same ratio in the two as the fat. The percentage of the dried matter of the stool which is protein is nearly the same in the stools of the different classes.

Ash.—It is well known that the ash represents a considerable part of the dried matter of the stools, but that in normal, pasty stools it is equal to two-thirds the fat is not generally appreciated. In loose stools about the same relation of fat and ash is preserved, while in watery stools the proportion of fat is relatively higher. The amount of ash in

TABLE 4.—Percentage Composition of Dried Matter

	Stools of Normal Consistency			Loose			Very Loose		
	Seven Patients Eleven Periods			Eight Patients Fourteen Periods			Six Patients Ten Periods		
	Average, %		Range, %	Average, %		Range, %	Average, %		Range, %
Fat	35.7	.....	(10.4- 81.0)	31.2	.....	(3.3- 56.7)	37.7	.....	(6.6- 61.3)
Neutral fat	.....	34.9	(12.2- 66.7)	.....	70.4	(10.6-160.)	.....	64.2	(17.2-103.)
Free-fatty acids	.....	10.8	(0. - 65.3)	.....	17.7	(0. - 35.6)	.....	27.5	(0. - 91.4)
Soap fats	.....	54.3	(14.7-173.)	.....	12.3	(0. - 47.2)	.....	8.3	(0. - 27.2)
Protein	25.8	.....	(15. - 36.5)	27.5	.....	(18.7- 44.4)	26.3	.....	(17.9- 50.6)
Total ash	24.8	.....	(13.8- 40.9)	21.0	.....	(11.3- 45.7)	18.7	.....	(14.3- 22.6)
CaO	.....	47.0	.....	.....	42.3	.....	.....	27.4	.....
MgO	.....	4.4	.....	.....	4.0	.....	.....	4.0	.....
P_2O_5	.....	29.1	.....	.....	27.3	.....	.....	19.7	.....
Cl	.....	1.0	.....	.....	5.6	.....	.....	9.2	.....
K_2O	.....	8.3	.....	.....	14.2	.....	.....	27.6	.....
Na_2O	.....	1.9	.....	.....	6.6	.....	.....	11.9	.....

some individual cases is interesting. In one normal stool it formed over 40 per cent. of the dried matter of the stool and in one loose stool, over 45 per cent.

When we study the distribution of the salts which make up the total ash it is seen that, while the percentage of the total varies, the actual amount of calcium is nearly the same in normal and loose stools, but is lowest in very loose stools; the quantity of all the other salts, notably sodium and potassium, however, is very greatly increased.

Residue of Dried Matter not Accounted For.—In going over our figures it was evident that there was a considerable percentage of the dried matter not accounted for as fat, protein and ash. This is indicated in Table 5.

TABLE 5.—PERCENTAGE OF DRIED MATTER OF STOOLS NOT ACCOUNTED FOR AS FAT, PROTEIN AND ASH

Stools	Dried Weight, Gm.	Sum of Fat, Ash and Protein, Gm.	Balance not Accounted for, Gm.	Per cent. of Dried Weight
Normal	8.75	7.55	1.20	13.7
Loose	12.95	10.32	2.63	20.3
Very loose.....	21.16	17.49	3.67	17.3

This unexplained residue varies greatly; in some stools it was only 3 or 4 per cent. of the total; in others it amounted to 25 per cent. of the dried matter of the stool examined. In a review of the literature of the past dozen years we have not found any attempt at explanation of what this unaccounted-for residue is. It is sometimes referred to as "other substances," but usually is entirely ignored.

Exactly what it is has not yet been determined by the direct method. The probabilities are that it is made up chiefly of the cellulose derived from the bodies of bacteria. Evidence of this is found in the carbon content of the dried organic matter after the extraction of the fat. As determined by combustion, the dried matter minus fat was found to contain about 43 per cent. carbon. As protein contains 52 to 54 per cent. of carbon, and carbohydrate but 44 per cent., this substance is probably chiefly carbohydrate. This carbohydrate is certainly not derived from the food. The sugar ingested is either absorbed or undergoes fermentation in the alimentary tract. It is true that many of our children were taking starch, some of them in considerable amounts. But in only exceptional stools could the presence of starch be demonstrated by microchemical tests, and then only in minimal quantities. It was in no case sufficient to account for the carbohydrate content of the stool. Furthermore, just as great carbohydrate content

existed in the stools of many children who were receiving no starch at all. The evidence therefore all points to cellulose derived from the bodies of bacteria as the chief factor in this dried matter unaccounted for.

The proportion of the stool made up of bacteria is great, making, according to various investigators, from 10 to 40 per cent. of the dried matter; in some constipated stools in infants it is estimated to have made up two-thirds of the stool.

TABLE 6.—RATIO OF INTAKE TO EXCRETION AND PERCENTAGE OF INTAKE LOST IN STOOLS

	Normal		Loose*		Very Loose†	
	Seven Patients Eleven Periods		Eight Patients Fourteen Periods		Six Patients Ten Periods	
Fat	12.4	....	23.1	....	40.5	....
Protein	7.7	....	14.9	....	25.2	....
Total ash....	40.0	(in urine)	46.6	(in urine)	84.3	(in urine)
CaO	67.2	Trace	70.2‡	Trace	79.0	Trace
MgO	56.7	Trace	66.0	Trace	100.0	Trace
P_2O_5.....	36.9	36.7	41.4	36.0	48.3	41.7
Cl	3.7	79.0	17.7	70.2	52.9	17.0
K_2O.....	15.4	54.9	37.9§	37.9	83.7	26.6
Na_2O.....	12.3	67.5	37.0	28.2	103.0	5.7

*In six periods the sodium and potassium distribution was not determined.
† Complete distribution of ash was determined in only four periods.
‡ Fourteen periods.
§ Eight periods.

Ratio of Intake to Excretion.—In the normal stool the loss of fat was but 12.4 per cent. of the intake, while in the very loose stools it reached 40.5 per cent. It is known that fat may be demonstrated in the stool when none is given in the food, it being derived from the intestinal secretions; but the amount is very small and from a nutritive point of view it is a negligible quantity. The loss of protein in the normal stool estimated from the nitrogen content represents but 7.7 per cent. of the intake. This shows how completely the protein of cow's milk is digested and absorbed by the average child. In the loose stools, calculating all the nitrogen as representing protein, the loss is 14.9 per cent. of the intake, and in very loose stools it is 25.2 per cent. This is not strictly true. In loose stools, and especially in watery stools, a considerable amount of protein present is not derived from the food, but is drained away from the body in the intestinal secretions. How much this is we are as yet unable to estimate, but it must be quite large. It is probable that although the infant with diarrhea loses over 40 per cent. of the fat which is given, he does not lose 25 per cent. of the protein given. This is incidental, but very important confirmatory evidence of

the value of protein feeding in diarrhea which has received so much support from clinical observations. When we study the distribution of the salts which make up the ash it is evident that they are not derived entirely from the food ingested, but that they represent a considerable draining away of salts from the body itself. In normal stools nearly four-fifths (76.1 per cent.) of the ash is calcium oxid and phosphoric acid, probably existing in the stool as calcium phosphate, while the proportion of chlorin and potassium and sodium oxids together form but 11.2 per cent. of the total. In the dry, formed stools the ash is often high, due to the bases combined with the fats as soaps.

In very loose stools we found calcium oxid and phosphoric acid to form but 47.1 per cent. of the total, but there was a great increase in the proportion of sodium, of potassium and of chlorin; together they make up 48.7 per cent. of the total ash, the chlorin being nine times, the potassium oxid three and a half times, and the sodium oxid six times the proportion in normal stools. This cannot be without significance.

Normally, 40 per cent. of the ash intake is lost in the stools; this is chiefly calcium phosphate, of which cow's milk has so great an excess. In very loose diarrheal stools there is lost 84.3 per cent. of the intake. The proportion of calcium phosphate shows but a moderate increase over that in normal stools, 79 as compared with 67.2 per cent. of the intake. The great increase in the total is made up of the other salts. The magnesium loss is 100 per cent., indicating that it very slowly enters into combinations in which it can be absorbed. The loss of calcium and magnesium occurs almost exclusively in the stools, only traces being found in the urine. Of the remaining elements, the loss in the urine must be considered in estimating the balances. Chlorin, potassium and sodium are normally present in the stools in relatively small amounts, but in the urine in large amounts. In diarrheal stools we find an enormous increase in the quantity present in the stools and a corresponding reduction in the amount eliminated by the urine. But the increase in the stools is so great as to create a negative balance of 10.3 per cent. in potassium and 8.7 per cent. in sodium. This indicates the loss from the body itself.

The ratio of the loss of salts to the intake is one of the most striking characteristics of loose, diarrheal stools and furnishes an important suggestion as to treatment. In attempting to supply this loss by hypodermoclysis it should be remembered that not only are water and sodium needed, but potassium and magnesium as well. With these facts in mind a better solution for use in hypodermoclysis can certainly be devised than a normal saline or than Ringer's solution.

This subject is still under investigation at the Hospital Laboratories and the foregoing is to be regarded in the nature of a preliminary report.

SOME STUDIES IN FAT INDIGESTION*

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The studies which we are carrying on at the Infants' Hospital in cases of chronic indigestion from fat do not yet include a sufficient number of cases to permit me to present a mass of statistical evidence from which positive conclusions can be drawn. It is difficult to accumulate evidence of final value in a clinical study of this kind. So many cases cannot be investigated as thoroughly as we could wish, and there are so many adventitious circumstances which interfere with the value of our conclusions, that I realize that the evidence they afford is at best but a general impression, not supported by real proof. At present, all I can do is to describe the method which we are employing, and to state the provisional conclusions which we have formed at the present stage of our investigations.

The diagnosis of chronic indigestion from fat is based on the fact that there is evident in these cases a marked intolerance of cow's milk fat. This intolerance shows itself in the inability of the child to take the amount of fat which the majority of artificially fed infants can take, without showing signs either of failure of fat absorption, or disturbance of digestion, or both. In other words, the cases of babies in whom the giving in the food of a moderate amount of fat is followed by the appearance in the stools of free fat or excessive soap, or in whom an increase in the amount of fat given in the food produces immediately symptoms of indigestion and nutritional disturbance, are classified and treated as cases of fat intolerance. In most cases the two conditions of indigestion and deficient fat absorption coexist.

The number of cases of fat indigestion treated in the hospital since it was opened on March 3, has been greater than the number of cases of indigestion from overfeeding, from protein, from carbohydrate, or with fermentation. This does not mean that this is the most frequent form of indigestion seen in infants. The cases received at the Infants' Hospital are, to a large extent, selected cases, chosen from a number of out-patient clinics, and referred to the hospital because they are not doing well. I think it safe to say that a great many of the worst cases come to us. The preponderance of cases showing fat intolerance means

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* Read before the New England Pediatric Society, Dec. 4, 1914.

only that this form of indigestion is the most serious, resistant and difficult to treat. The majority of the patients, when received at the hospital, showed the most extreme degree of malnutrition, being in appearance typical of atrophy, some of them being actually moribund. The number of cases studied was actually no more than thirty-five. This number is so small that it seems hardly worth while to present the results of the studies in statistical form, with tables and figures.

Cases of fat intolerance show a certain constancy in their clinical behavior. This constancy, however, is not found in the clinical symptoms of indigestion, but rather in the manner of their response to attempts to feed them. I mean by this that there is not a constant or typical macroscopic appearance of their dejecta. The movements may or may not look undigested, with soft so-called "fatty curds," or may be white, or brown, or green. They are apt to appear abnormal in some respect, but may not. Vomiting may be absent, or occasionally present, or it may be the only symptom of overfeeding with fat. The typical feature of fat indigestion may be summarized in these words: inability to gain with fat, and inability to gain without it. I mean by this, that if these babies are given a quantity of fat so small that they show no signs of fat intolerance, they lose weight or fail to gain; when more fat is given they show signs of fat intolerance and continue to lose. One peculiarity of these cases we have noted again and again — when the quantity of fat given is increased, in the hope of obtaining a gain in body weight, the babies are apt apparently to respond. They show a gain in weight, and the signs of fat intolerance do not develop at once. Excessive soap, however, appears in the stools, while they are gaining in weight, and then, often after many days, suddenly, within a day or two, they lose all the weight they have accumulated, and more. This phenomenon is so frequent and striking that at the hospital it has come to be commonly called a "blow-up." These "blow-ups" are usually attended by a reappearance of such symptoms as vomiting, bad movements, or even diarrhea. Sometimes they have been accompanied by marked signs of collapse, with cold extremities, cyanosis, and slow pulse. In two of our cases, such "blow-ups" have been fatal.

We have been, and still are, studying these cases by giving various foods, controlling our observations by frequent microchemical examinations of the stools. I realize that such a method of study cannot reach the bottom of the nutritional questions involved, and at best can only give us a clinical basis for procedure. We must look to more complicated studies on metabolism for a final decision.

The points which we have studied are the following:

1. Are there any striking predisposing causes for fat indigestion?

2. Can we successfully compensate for deficient power to digest and absorb fat, by increasing carbohydrate or protein, and if so, to what extent?

3. Is the microchemical examination of the stools for fat a reliable guide to the feeding of these infants, and if so, to what extent?

4. What are the relative values of maltose and lactose as the carbohydrate element in these cases?

5. What are the relative values of precipitated casein and unmodified protein in these cases?

6. What is the value of lactic acid milk in these cases?

The conclusions we have reached have been the following:

1. In looking over our records I have been much struck by the frequency of some evidence of tuberculosis or syphilis in these cases, especially tuberculosis. In two fatal cases tuberculosis was found at necropsy, and in quite a number of others there were some signs, either a tuberculin reaction, signs in the chest or a suspicious radiogram. I am inclined to think that tuberculous babies are especially prone to fat intolerance.

The study of the previous feeding in those cases gave a very unexpected result. In extremely few instances was there any history of overfeeding with fat. In general, the history in these cases is one of overfeeding with carbohydrate. Milk mixtures with excessive sugar, especially cane-sugar. condensed milk, and the various carbohydrate foods, are the usual previous feeding. In a large proportion of cases the previous history suggested carbohydrate indigestion, the clinical features being frequent green irritating movements, vomiting, regurgitation, and much gas and colic.

This finding is interesting in connection with our theories as to the cause of fat intolerance in artificially fed babies. There is some difference of opinion as to whether, in these cases of atrophy, the first injury comes from the nature of cow's milk fat, from the nature of the cow's milk salts, or from excessive carbohydrate fermentation. Our evidence would point to the last of the three. Of course, feeding with various carbohydrate patent foods, or with excessive sugar, is such an extremely common method that the frequency of its general use may account for the frequency of its occurrence in our series. Nevertheless, I am strongly inclined to the view that it is an important cause of failure to digest and absorb fat. These infants after they entered the hospital usually presented an entirely different picture from that described in their histories. They took care of all the carbohydrate we gave them, but they showed this marked intolerance of fat. The effect of long-continued fermentation from overfeeding with

carbohydrate may well be a failure of the power of digesting fat, the carbohydrate injury being primary, but the fat indigestion coming to dominate the picture.

2. In answer to the question as to how far we can compensate for deficient fat digestion by the giving of more carbohydrate and protein, I would say, to a very slight extent. Some cases of fat indigestion, the milder ones, yield readily to proper feeding, and the babies gain weight for a long time with very little fat, or even no fat, in their food. These, however, are babies who seem to have a low caloric requirement; at any rate the quantity of carbohydrate and protein given is not excessive. The majority of the severe cases, such as we get at the hospital, will not gain on moderate quantities of carbohydrate and protein as a substitute for fat. If these quantities are increased, signs of indigestion quickly appear. We have had several cases in which edema and tetany have suddenly appeared, and it is curious that they were all cases on a food relatively high in protein.

3. As to the value of the microchemical examination of the stools, I believe that frequent examinations of the stools for fat are absolutely essential to the proper treatment of these cases. No case of "blow-up" from fat has occurred without the finding of an excess of soaps (and sometimes free fat) in the stools before the occurrence of the upset. The important question, however, is whether the finding of an excess of soap in the stools is a positive indication for reducing the fat in the food. A certain number of babies would not gain in weight until the quantity of fat was increased to such an extent that excessive soap was present in the stools. In some of these the excess of soap lessened and finally disappeared. Others continued to gain until their discharge from the hospital without any lessening in the excess of soaps found. Excess of soap is not incompatible with prolonged gain in weight. On the other hand, in so many cases in which the patients were gaining in weight and showing excessive soap in the stools a "blow-up" did occur, that there is undoubtedly a great risk in continuing to feed the babies so much fat. Moreover, I find that some of the patients that were gaining at the time of discharge with excessive soap in the stools, experienced a "blow-up" subsequently, after quite a long time. Therefore I believe that, in cases in which the patients are gaining, one should make frequent examination of the stools for fat, and if the quantity of soap does not lessen or increases, the fat must be cut down, even if the babies have to undergo a further period of failure to gain, or even of loss in weight. Free fat in the stools should always be a positive indication for cutting down the quantity of fat in the food.

4. The question of the relative value of maltose and lactose as the extra sugar added in cases of fat intolerance was studied as follows:

In cases in which there was intolerance of a definite quantity of fat when lactose was used, a fresh start was made, maltose being used instead as the extra sugar, and the fat was increased in exactly the same way as before. If the babies appeared to be able to gain on maltose, the sugar was changed back to lactose, without any other change, in order that we might see if they became worse. In some cases, when intolerance of a certain quantity of fat developed with lactose, the extra sugar was changed to maltose without reducing the fat, in order that we might see if their tolerance of fat improved.

We have concluded that, in general, cases of fat indigestion do better with maltose than with lactose, and we believe that in the feeding of these patients maltose is the preferable extra sugar. Nevertheless, the evidence is somewhat contradictory. The conclusion supported by the most consistent evidence is that patients with fat intolerance will gain weight and do well on a smaller quantity of fat when maltose is used. A number of patients that would not gain before the fat was increased sufficiently to produce signs of fat intolerance, did gain and do well on a smaller quantity of fat when maltose was used. And in some of these, changing the fat back to lactose caused a failure to gain in weight. No patient did better on lactose than on maltose. There is much less evidence, however, that the use of maltose actually increases the tolerance of fat. It is true that in some cases in which the fat was gradually increased a second time, with maltose in place of lactose, an increased tolerance for fat was found. This occurred, however, no oftener than might be accounted for by a general tendency toward improvement after a period of diminished quantity of fat in the food. In other cases, the fat intolerance developed with the same quantity of fat with maltose as with lactose. Some patients who showed increased tolerance for fat with maltose showed less tolerance when the sugar was changed back to lactose, but this has not occurred often enough to seem very significant.

I believe that the chief value of maltose in these cases is that it is the best carbohydrate to replace the deficiency of fat — to meet the caloric need created by the fat intolerance. The action of maltose in this respect may easily be explained theoretically. Maltose is split during the process of digestion into the two molecules of the monosaccharid dextrose, of which it is composed. Dextrose is probably less fermentable and more easily absorbed than either the galactose of lactose or the levulose of cane-sugar. It has the further merit of being the only carbohydrate which, after absorption, can be immediately utilized for energy production, without undergoing glycogen storing.

It is possible, but by no means evident, that the maltose actually aids the power of digesting and absorbing fat. If this is the case, it

could be explained easily under the theory that sugar indigestion and fermentation is a predisposing cause of fat indigestion. The maltose, being so easily absorbed, leaves behind less fermentable residue, and in consequence, we have less sugar fermentation and better digestion of fat. This, however, is at present only speculative. It would account for the improvement in fat tolerance seen with maltose, but this, as I have said, can also be accounted for by a tendency toward improvement sometimes seen with careful regulation of the amount of fat given in the food.

5. The value of precipitated casein was studied in the same way as maltose by increasing the fat with a definite percentage of unmodified protein, and then with the same percentage of precipitated casein, and by alternating the two forms of protein with the same percentage of fat. Albumin milk was not used; as it is a combination of precipitated casein and lactic acid milk, we believed that its use would not throw so much light on the questions in which we are interested as would the use of its essential elements separately. I am quite ready to admit that albumin milk may be a better food for these infants than any we have tried. But it appears to me to be a sort of shotgun prescription, based on somewhat mixed theoretical conceptions.

The question of the value of precipitated casein is of interest chiefly in connection with the possible rôle of the cow's milk salts in cases of fat intolerance. The essential features of precipitated casein are: first, that its use in place of fat-free milk in modification enables us to diminish the mineral salts without diminishing the protein; second, that it enables us to diminish the lactose to a very small amount, and third, that the casein, being already precipitated in a finely divided form, does not have to undergo precipitation in the stomach. The last feature would not appear to have any direct bearing on the question of fat indigestion, unless there was also protein indigestion. In such a case, more protein might be digested and absorbed with precipitated casein, but we have no evidence pointing toward this. On the contrary, patients that developed signs of protein intolerance with fat-free milk did no better with precipitated casein. The diminution in the lactose with precipitated casein mixtures may be a feature of value, but in view of the effect of changing the extra sugar from lactose to maltose, it does not seem likely that the small quantity of lactose in the fat-free milk is harmful in many cases. If precipitated casein showed a marked superiority in these cases, I should be inclined to attribute it to the diminution in the cow's milk salts.

But it did not show a marked superiority. Here again the evidence is somewhat contradictory. The majority of cases in which precipitated casein was tried did not do better than with the regular form of

protein. Fat "blow-ups" occurred with the same quantity of fat with precipitated casein as with unmodified protein. We have as yet had no case which gave evidence of being able to digest without symptoms more protein with precipitated casein than with total protein. On the other hand, we have had patients who gained better on precipitated casein than on total protein. Some continued to gain when the form of protein was changed back again; others did not gain so well. We have had one case in which the fat tolerance was found increased when precipitated casein was substituted for the usual form of protein, and in which fat intolerance developed when the protein was changed back again.

I cannot conclude that precipitated casein may not be of value in some cases of fat indigestion. In the majority of cases it promises no advantage over the usual protein. Our results have been rather against the rôle of the cow's milk salts in producing fat indigestion, but I believe this to be still an open question, in view of the opposite results which many observers have published.

6. Lactic acid milk has not been sufficiently studied to afford the drawing of even provisional conclusions in fat indigestion. We have not as yet found evidence of its value. We have had cases of protein indigestion develop under its use.

I might give the following summary of the ideas which we now hold at the Infants' Hospital as to the treatment of these severe cases of fat indigestion:

The milk modifications used must be low in fat, average in carbohydrate, comparatively high in protein. The extra sugar should be maltose. A certain number of the milder cases will do well on this treatment. Severe resistant cases are those in which the patients cannot gain on a low quantity of fat and cannot tolerate an increase. A large number of cases are so severe and resistant that they can be saved only by human milk. Breast-milk will save most of these cases, even the severe ones, if used in time. It should always be used in resistant cases, whenever it can be obtained. Even a little breast-milk is of value, and may save a patient that would otherwise be lost. After a period of breast-milk feeding, many cases are found no longer severe and resistant to artificial feeding. If breast-milk cannot be obtained, the feeding is very difficult and the outcome uncertain. Excessive increase of carbohydrate or protein will not help these severe cases, and may do harm; I do not believe that more than 7 per cent. carbohydrate or 3 per cent. protein should be given. Whey mixtures are of no help except sometimes in very young babies who vomit curds; they may do harm. Giving the protein in the form of

precipitated casein may be tried, and may help in some cases. There is not sufficient evidence of its value to indicate its use as a routine.

The only way we have of managing these resistant cases without breast-milk is to keep the fat low, and we must be prepared for a period of loss of body weight which may be prolonged. If they begin to gain when the fat is increased, it is no sign of permanent improvement; they may go to pieces at any time. Frequent examinations of the stools for free fat and excessive soap must be made. In the presence of free fat, or in the continuous or increasing presence of excessive soap, the fat should be reduced, even if the baby is gaining. If a "blow-up" occurs when the fat is increased, the fat in the food should be reduced to zero, and then worked up again, slowly. Frequent "blow-ups" diminish the tolerance for fat. The best hope of eventually obtaining an increase in tolerance of fat sufficient to permit a gain in weight is to avoid overfeeding with fat for a long time, even if much weight is lost.

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A STUDY OF CERTAIN CASES OF INFANTILE DIARRHEA DURING THE SUMMER OF 1914*

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The problem of the diarrheal disorders of infancy, in spite of a tremendous amount of study, is by no means solved. A great step in advance has been the contribution of Finkelstein, who has described a large group of cases showing them to be caused by abnormal changes of the food within the intestine, his "alimentary intoxication." Abroad, this idea has met favor among many of the foremost pediatricians, and the tendency there seems to be to class almost all diarrheal cases as distinct food disturbances, though some brilliant clinicians such as Czerny refuse to recognize the condition.

In this country, sectional differences in observation prevail. In Chicago and in the middle west one undoubtedly sees in the majority of diarrheal cases the typical types described by Finkelstein. In the east a relatively larger proportion of cases of infectious diarrhea have been reported. The researches of Kendall and his associates in the Boston Floating Hospital show very conclusively that in certain years bacillary dysentery is a frequent type of diarrhea seen in the infants in the hospital.

After reading the studies of Finkelstein and then reading the very antithesis, the work of Kendall, both reporting hundreds of cases, one must conclude that both are right, and that the difference in the views as to the etiology of these disorders is simply due to a difference in the material seen. For instance, Kendall and Smith[1] in 1911 report cases in children of bad diarrhea greatly resembling dysentery, but associated with great numbers of gas bacilli in the stools. As the gas bacillus is injured by lactic acid, the treatment instituted was the feeding of buttermilk. Under this treatment the patients improved markedly. When carbohydrate was fed, as lactose, however, the condition became worse, and when the carbohydrate was removed the patients clinically improved and the stools gradually became normal. Further, since the gas bacillus grows only poorly on protein the fact that Eiweiss-Milch is made up of high protein, lactic acid and low carbohydrate led

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* Read before the Congress of Pediatricians of the Middle West held in Chicago, Oct. 29, 1914.

* From the Northwestern Medical School and the Sarah Morris Hospital for Children.

1. Kendall and Smith: Boston Med. and Surg. Jour., clxiv, 307.

Kendall to suggest that perhaps a certain number of the cases classed by Finkelstein as food disturbances, improving under albumin milk therapy, might be cases of gas bacillus infection of the milder type. With these ideas in mind we undertook to study our material at the Sarah Morris Hospital this summer from the point of view not only of food disturbances, but also of infectious diarrheas.

Our cases of severe diarrhea up to September number twenty-two. These cases divide themselves into three groups, each of which is

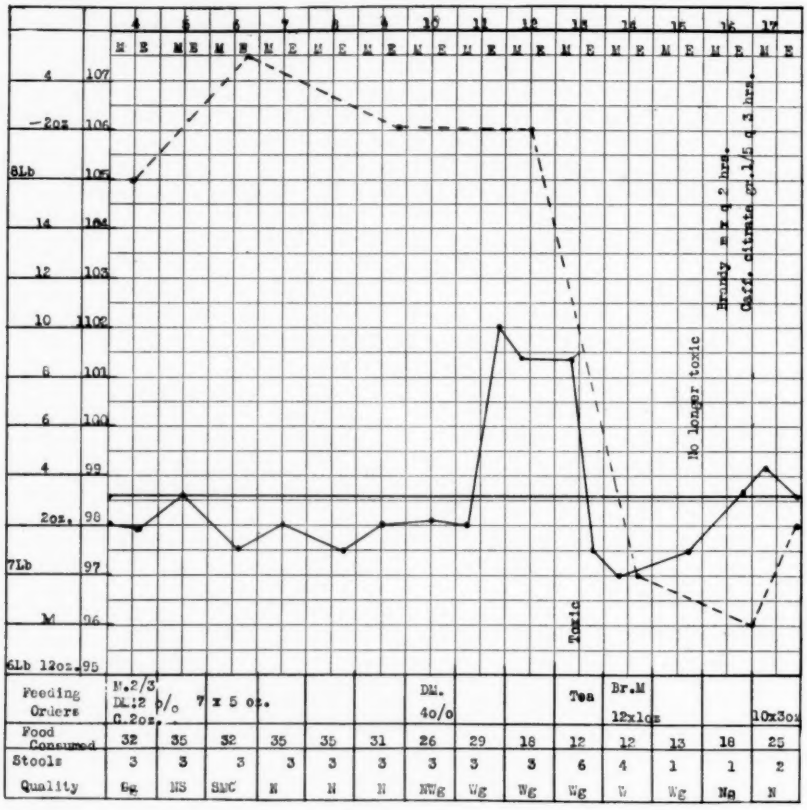

Chart 1.—J. S.; diarrhea from alimentary disturbances. In this and the following charts the solid line indicates temperature and the broken line indicates weight. Under feeding orders, Br. M. indicates breast-milk; C, cream; D. M., dextri-maltose; E. M., Eiweiss-Milch; M., milk. Under stools, B indicates blood; b, brown; c, curds; g, green; M, mucus; N, normal; S, soft; W, watery.

illustrated by one of the accompanying charts: (1) food disturbances; (2) infectious diarrheas, and (3) parenteral infections. By the latter we mean such cases of diarrhea as occur secondary to infections outside of the intestinal tract as a bronchitis, an otitis media or a coryza.

It was somewhat surprising to find that but two of the twenty-two cases of severe diarrhea could be classified definitely as belonging to the group of food disturbances. These two showed the picture of the alimentary intoxication described so clearly by Finkelstein — a rise in temperature, a sharp drop in weight, watery, green stools, perhaps even bloody, skin of a pale muddy color, fixed staring eyes, tireless deep breathing, an enlarged liver, leukocytosis and glycosuria.

As an example let us take the case of J. S. (Chart 1) aged 3 months. The child was a "feeder" in the hospital, being on two-thirds milk with 1 ounce cream and 2 per cent. dextri-maltose. When the

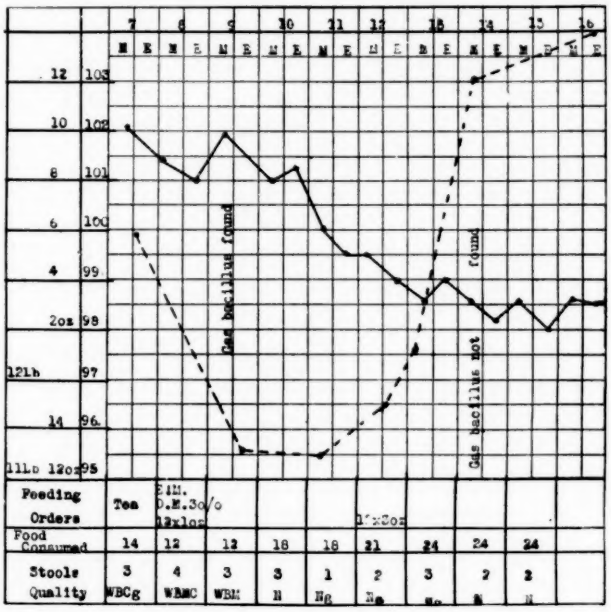

Chart 2.—S. P.; diarrhea with gas bacillus infection.

carbohydrate was increased to 4 per cent. the stools became watery, the child developed a fever, the weight curve dropped and all the above-mentioned symptoms appeared except glycosuria. Physical examination was absolutely negative as regards any foci of infection, and bacteriologic examination of the stools showed no abnormal organisms. Under tea diet for twenty-four hours the acute symptoms disappeared and with small doses of breast-milk the child made a rapid recovery.

In two cases the gas bacillus was found. A typical example is that of S. P. (Chart 2), aged 1 year. He had never been a very strong child, but had had no diarrheal attacks. He was never breast-fed, but received milk, oatmeal water, crackers and cereals. The child had been

ill one week when admitted. The onset was acute, according to the mother, with fever, chilly sensations, headache and diarrhea, six or seven stools per day being passed, soft, green with curds, mucus and blood. He had had a cough for some time and had lost weight since the onset of this attack. Physical examination showed an emaciated child presenting somewhat the appearance of an alimentary intoxication. The mentality was dulled, the respirations rapid and the skin hot, dry and inelastic. Other than this the physical examination was negative, except that the liver was palpable one finger's breadth below the costal margin. Examination of the chart shows that the temperature did not fall on withdrawal of food, that the loss of weight did not cease and that the stools did not at once improve. Finkelstein definitely lays down the law that a fever not disappearing within twenty-four hours or at the very latest forty-eight hours after the withdrawal of food is in the majority of cases not to be considered an alimentary fever. An alimentary intoxication is thus out of the question. Physical examination showed no foci of infection to account for the fever, but bacteriologic examination of the stools revealed the presence of the gas bacillus. Under the treatment instituted, Eiweiss-Milch, the fever slowly came down, the stools improved, the weight curve ascended and the gas bacillus disappeared from the stools. In this case, then, had we not examined the stools bacteriologically we might, after seeing the improvement with Eiweiss-Milch, have classified the case as a food disturbance.

It is striking that the greatest number of our cases were associated with foci of infection in other parts of the body, that is, the parenteral infection group. Whether we were justified or not in concluding that the parenteral infection was the cause of the diarrhea is an open question, but at any rate, the coexistence of the two conditions is certainly worthy of note. This corresponds with the observances of Finkelstein, that is, that the parenteral infections are by all means the most important factor in the production of food disturbances. Of the parenteral infections there were eighteen cases in our group.

A typical example is the case of M. M. (Chart 3) aged 4 months. She had been a healthy baby until the present time and had had no illnesses or diarrheal attacks. The child was breast-fed for two months and also received the bottle, as the mother had to work. For the last two months the child had received 4 ounces of certified milk diluted with an equal volume of water whenever she cried. Four days before admission she was taken acutely ill with fever and diarrhea, she coughed and sneezed, had a temperature of 102 F. and lost some weight. The stools numbered six or seven per day, were soft, green and contained mucus and curds. Physical examination was absolutely

negative as to any organic changes other than that the liver was palpable one and one-half finger's breadth below the costal margin. The child, however, showed the picture of a typical intoxication with dulled, fixed eyes surrounded by deep circles, rapid feeble pulse, very feeble cry, deep respirations, an ashen dry skin and generally toxic appearance. On examination of the chart we find the cardinal symptoms diagnostic of an alimentary intoxication present, the sharp drop in weight associated with fever and bad stools, but we also find the

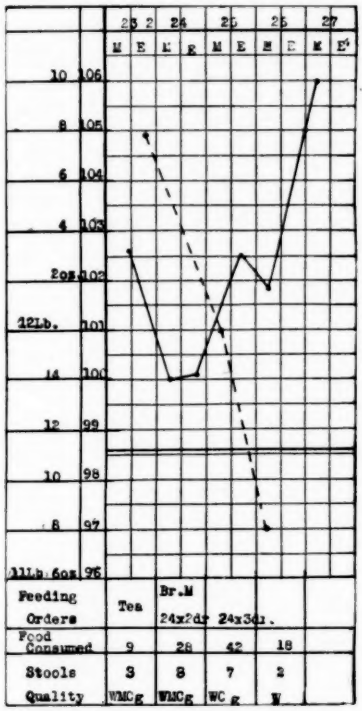

Chart 3.—M. M.; diarrhea associated with parenteral infection (bronchial).

cardinal symptoms of a *primary* food intoxication absent, for on the withdrawal of food for twenty-four hours the temperature does not fall by crisis or the symptoms improve. So in this case alimentary fever is easily ruled out. The cultures from the stools were negative, and, as a definite enteral infection was absent, we must assume that the fever was due to the primary bronchial infection and that the food disturbance was secondary.

Another example is the case of G. H. (Chart 4), aged 7 months. The child was in good health up to the time of admission. She had had no diarrheal attacks before. She was breast-fed for two months and then given a milk mixture of milk, water and sugar. Three weeks

before admission the child was taken ill with diarrhea. This ceased and then a few days before admission commenced again with fever, vomiting and from six to ten watery, green stools per day containing mucus and curds. She lost 2 pounds in weight and has had a chronic cough. Physical examination showed a sickly-looking but not markedly toxic child with rapid pulse and inelastic skin. Dulness was present over the right upper lobe. The chart, as in the previous case, shows first a fever, then a loss of weight and bad stools continuing in spite

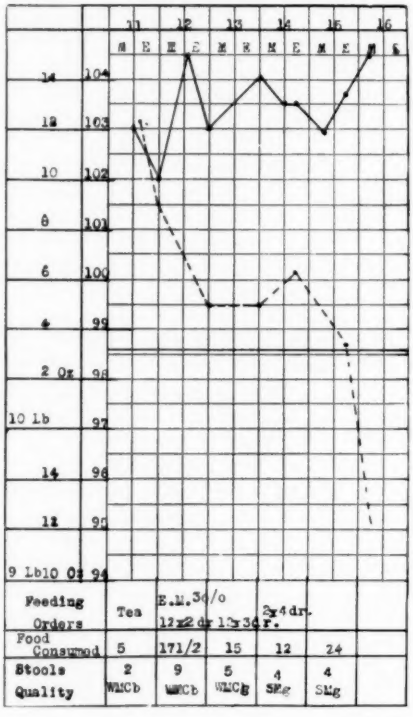

Chart 4.—G. H.; diarrhea secondary to bronchpneumonia.

of the withdrawal of food. Secondly, a careful bacteriologic examination of the stools failed to show any pathogenic organisms. Examination of the patient showed a pneumonia. We must assume, then, in the absence of a primary food disturbance, as shown by the failure of the fever to fall on the withdrawal of food, in the absence of a specific intestinal infection, that the pulmonary infection was the primary disturbance and the diarrhea secondary. The post-mortem examination showed a bronchopneumonia of the upper right lobe and a hypostatic pneumonia of the posterior right lobe. Bacteriologic examination demonstrated the presence of pneumococci in the diseased lung.

In our limited study this summer we have tried to consider every case in the broadest way possible, taking into consideration all of the most important factors in the causation of diarrheal disorders. Studied in this way, out of only twenty-two cases, already three groups emerge, the group of true food disturbances, the group of true intestinal infections and the group of parenteral infections. Why we saw no dysentery is difficult to say. Not a single case studied this summer even clinically resembled the dysentery cases seen in Boston, not even in the nature of the stools, for the gas bacillus cases were not severe enough to be confused clinically with typical dysentery. It is striking that in most clinics abroad and here in the middle West, the diarrheas do not belong to the definite infectious group as they do in the East. In explanation we are tempted to fall back on the work of Brenneman, who settled the great dispute between Europe and America as regards curds in the stools, by showing that *all* observers were correct and that the difference in results was due to the use of boiled milk abroad and raw milk in America. Is it not possible that this difference also explains the discrepancy as regards diarrheal cases? Here in the middle West, we are rather inclined to follow the German teaching and boil our milk. In the East the tendency is to use it raw. The boiling of milk must of course be a great factor in cutting down the number of dysentery cases seen here. That gas bacillus infections occur even with the use of boiled milk is not surprising since the mere boiling, as ordinarily practiced, is not sufficient to destroy the spores of the gas bacillus. In the three groups of cases brought out here, we claim no originality, as these groups have been noticed for some time in the European clinics. We shall be satisfied if we have shown that one must not treat his diarrheal cases too dogmatically, that one must study them broadly, open-mindedly and that above everything else, each patient is a patient to receive individual study and care and treatment.

In conclusion we wish to express our thanks to Drs. Abt, Hess and Lackner, and to our associate, Dr. Jampolis, for the opportunity of studying these cases.

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PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE ON NOSE AND THROAT WITH REFERENCE TO CHILDREN

THE RELATION OF TONSILS AND ADENOIDS TO THE DEVELOPMENT OF THE CHILD

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The subject of tonsils and adenoids in children is always interesting to the pediatrist, especially from the point of view of their relation to the mental and physical development of the child, and has received considerable attention during the past year.

In the first place, the tonsillar and adenoid tissues are physiologic structures, and their relation to the mental and physical development in children is of extreme importance. The position of the tonsil is such that, owing to its size and location or the fact that it is imbedded or adherent or pathologically altered, it will interfere with the mechanism of phonation, and therefore in early life bear an important relation to the development of speech, and if diseased it will in turn affect physical development.

These glandular structures are apt to be large in children, so that, at the formative age, in which the child is learning to talk, any abnormality of this structure or any interference with the mechanism of phonation may cause defects of speech, or rather, peculiarities of speech, which will be detrimental to the development of the child.

Children, as well as adults, are very impressionable and extremely sensitive to ridicule, and a child is very quick to notice that it has difficulty in saying certain words correctly, or that it has some defect of speech caused by the presence of the tonsil or adenoid, which gives a peculiar intonation. To the child its own voice is natural, and it is only by comparison with others that it notices the peculiarity. Such peculiarity may lead to so-called backwardness, not that the child has any deficient mental capacity, but that on account of the interference with the mechanism of phonation and the fear of ridicule and of being laughed at by its little playmates or schoolmates, the child would rather admit that it does not know than to use its voice and be the subject of ridicule. Such defects are frequently observed in children from 3½ to 6 or 7 years of age.

The same is equally true of the adenoid structure. We know that children who have a large adenoid growth and who are mouth-breathers, have very poor enunciation. They have lack of nasal reso-

nance and difficulty in enunciating, especially in certain sounds and words. Besides, there is a certain mental hebetude observed in children who have this adenoid growth. There is also a peculiar relation to the mentality of the child suffering from enlargement of this gland. Drs. Harrison Allen and J. Solis Cohen were the first, I believe, to call attention to the intimate relation of this gland structure to the brain and meninges.

The child's mentality may be normal, but it would require more effort to attain development in such a child than in one in whom the adenoid structure does not exist, or in whom it is not obstructive.

The child who has enlarged adenoids frequently shows a backward manner, timidity, lack of confidence and in some instances, on account of the interference with the eustachian tube and middle-ear involvement, feels an uncertainty as to equilibrium, is a little uncertain in his gait and feels at a decided disadvantage. This child is also handicapped by the facts that nasal respiration is interfered with, the respirations are entirely through the mouth, and the physiologic process of aeration does not fully take place. This in itself renders the child below par in its physical condition and handicaps it mentally.

While the defects in speech, which are purely mechanical, are not exactly the same as in the enlarged and imbedded or adherent tonsil, yet the effect on the child is practically the same. The child is unable to recite as the other children do, and notices very quickly the ridicule of its classmates, and besides, I am sorry to say, frequently the impatience of its teachers and also its parents. Some children are discouraged by comparisons.

With the removal of the adenoid tissue early in life and a little training on the part of the parents and teachers, it will be found that the child's capacity is equal to any other, and that the handicap was purely a mechanical one.

Usually the pharyngeal tonsil attracts the general practitioner's or specialist's attention only when it is the site of some pathologic process or when from its physiologic growth it becomes sufficiently large to obstruct nasal respiration and interfere with the development of the nasal and facial bones.

In early infancy the tonsil is rarely affected, but in early childhood it too often causes trouble mechanically and systemically.

The tonsil becomes pathologic only when its presence injures the individual, either locally or generally, not because some one discovers a pair of tonsils in that throat. The submerged tonsil, which may be quite small, is more liable to be doing harm than the fairly large, free tonsil. It is only in the last few years that the tonsil has been judged pathologically otherwise than from its size alone. The tonsil that is

more or less submerged is the one that nearly always is to blame for the infective processes about this region and in the neck, and from the neck to the general system.

A submerged tonsil that extends well up into the velum, diseased or not, may cause interference with the normal function of the eustachian tube, and, indirectly, with the middle ear, producing tubal catarrh, or one of the acute or chronic catarrhal or suppurative inflammations of the middle ear. By pressure alone it will interfere with hearing, even before its presence has caused inflammatory action. The tubal adenoid, that portion which sometimes is found in the eustachian orifice and often overlooked in operation, may be the direct cause in early life of serious ear involvement later.

The imbedded tonsil and the adherent tonsil also affect the child's general physical condition, as we all know, owing to the fact that the crypts and pockets formed behind such tonsils always permit of absorption into the lymphatic system of toxic material from the tonsil, which interferes with the general health and physical condition, and in turn would necessarily create a mental handicap. The child is below par, peevish, fretful and irritable, and lacks the energetic vitality of childhood.

The adenoid gland structure is particularly susceptible to inflammatory action and the slightest inflammatory change in this structure will produce in children marked rise in temperature with all the associated febrile phenomena. Frequently we have to deal with febrile conditions in children in which there is no apparent cause for the symptoms present, and the cause of such temperature, with the accompanying systemic phenomena, could be traced directly to the inflammatory condition of this adenoid structure. In any case in which there is the slightest infection, with inflammatory condition of the adenoid structure, the systemic phenomena are all out of proportion to the local cause; that the gland seems to rapidly absorb any toxic material, and that the temperature suddenly rises before there is any very marked constitutional effect.

Children with adenoid structure are more susceptible to cold and the diseases of childhood than those who do not have it, and the symptoms produced by the cold are aggravated in proportion to the amount of gland structure present.

It is vastly important, then, in many instances, not only from a point of view of physical development, but from a point of view of mental development, that these mechanical interferences with phonation such as an imbedded or enlarged tonsil or the obstructive adenoid, be corrected early in life, before habits are formed and fixed; otherwise the child grown to adult age will go through life handicapped both

mentally and physically. Extreme care should be taken in correcting these defects that the muscular structure of the soft palate and pharyngeal pillars are in no way injured, and thereby prevent the formation of any scar tissue which would involve the mechanism of phonation later in life.

Max Toeplitz[1] gives the results of five hundred examinations of the nose and throat in an institution for delinquent boys. To sum up the results of these 500 examinations, 351 boys were diseased, 106 had enlarged tonsils, 89 enlarged adenoids and 116 were combined cases. Of these, 292 required operation, 23 refused it, 24 were operated on by radical methods.

Because of the apparent large number of operations, it was decided not to touch soft adenoids or small tonsils. As a result, 40 per cent. of the cases treated by the physician during the year 1910 were attributed to the presence of adenoids and tonsils. The operative work was then extended in 1911, and 18.6 per cent. of the cases treated were traceable to the nose and throat.

According to T. F. Harrington, adenoids and tonsils will heal themselves in four out of five cases if the child is given plenty of outdoor air. In view of this, 300 boys were reexamined after a year's stay under the most hygienic conditions. It was found that in only six of these had the tonsils and adenoids disappeared; that four not previously affected were now suffering, the remainder had finally to come to operation. At the end of 1912 the general improvement of the hygienic status was marked, this being directly due to the operative work in 1911.

Arthur M. Corwin[2] points out that beside the morbid adenoid there is no other affection in childhood that is so common and far-reaching in its malign influence on comeliness, comfort, reliability and individual usefulness. He states that symptomatic hypertrophy of adenoids occurs in from 25 to 35 per cent. of all children between 3 and 10 years of age. It is, however, the direct and remote results of their abnormal presence on mental and moral integrity that he specially deals with. Among four hundred children at Bologna, Bonazzolo found that 141 displayed great lack of the power to concentrate attention, and therefore were backward students. In all but twenty-four of these, adenoids existed, and the twenty-four without them had nasal obstruction from some other cause. These children were neurasthenics. They are duplicated by the thousand in every school community as intellectual dwarfs.

In New York it was found that in a school population of 650,000, 30 per cent. of the children were about two years behind their grades,

1. Toeplitz, Max: Med. Rec., March 14, 1914.
2. Corwin, Arthur M.: Illinois Med. Jour., October, 1914.

and that 90 per cent. of these were delinquent because of removable eye, ear, nose and throat lesions. Cronin found, in New York schools, 150 marked defectives who were very backward in their studies and incorrigible in character; 137 of them had enlarged tonsils and adenoids. These were removed, and in six months the children were reexamined. All were doing well in studies, and their characters had undergone marked improvement.

It has been estimated that 40,000 children annually in Minnesota have adenoids that retard them one year in work.

In the United States 20,000,000 children constitute about 20 per cent. of the entire population. Of these twenty million children it is estimated that 75 per cent. suffer from remediable defect, more or less formidable, six million of them having operable adenoids.

The lack of attention, aprosexia, and lowered power of memory, resulting from typical adenoid obstruction and irritation are responsible for an enormous amount of backward and deviate mental development originating in infancy. The child is unable to apply himself to his prescribed work. Thus handicapped he falls behind his fellows and fails to catch up; he is accounted a dunce; he is punished by his teachers and parents, ridiculed by his mates, and soon finds other matters to take his attention. He grows sullen, apathetic or mischievous, and is considered incorrigible and a nuisance.

From a modern point of view, hypertrophy of the lymphatic ring of the upper air-passages, together with high arched palate, hypertrophy of the thymus with the associated deviation of other structures from the normal are considered among the stigmata of degeneracy and therefore to be referred to the same hereditary or acquired influence that results in hypoplasia in general. Certain it is that the hypoplastic infant is peculiarly afflicted with hyperplasia of the glands in question. The hypoplastic child, fundamentally unstable and still further handicapped by enlarged tonsils and adenoids, with their attendant train of evils, is prone to respond nervously in an exaggerated degree to harmful environmental influences and needs careful study and attention to insure the advancement of which he is in a great number of instances capable.

Corwin emphasizes the fact that a multitude of children with normal brains and normal means for developing them, if denied proper surgical attention, will suffer deterioration of their normal gray matter, and therefore of mental force. And though they may not graduate into criminals or degenerates or public dependents, they will be seriously handicapped all their lives.

THE TONSIL OPERATION IN CHILDREN

T. B. Layton[4] states that while there is much discussion as to the relative merits of tonsillotomy and tonsillectomy, we have not taken time to determine whether too many operations are performed. While we do not know the function of the tonsillar tissue, we have good reason to believe that it forms an early and important line of resistance to infection. The presence of hypertrophy is not alone sufficient ground for operation, as the proper care of the teeth, training in nasal breathing and the working out of a correct hygiene will frequently obviate the necessity for operation. He feels that the dangers from anesthesia, infection, hemorrhage and traumatism are real and not to be ignored in determining on operation, and that all patients operated on should receive prolonged and thorough aftercare. When the throat condition is part of a general lymphatic hypertrophy little may be expected from operation, and it is wise to operate in no case in which the temperature exceeds 99 F., as in this way one may usually avoid complications incident to beginning infectious diseases. He knows of no operation by which so much good is so easily done in carefully selected cases and urges against indiscriminate operation as a means of needlessly bringing this procedure into disrepute.

Thomas R. French[5] deplores the indiscriminate enucleation of the tonsils and offers a method for making a differential diagnosis which consists in making an exploratory section of one of the tonsils after the patient has been etherized for operation, and this section is immediately examined in a brightly lighted field under a finely ground loupe, with a magnification of from five to ten diameters. If it is found to be free from disease, the remainder of the gland and the one on the opposite side are both removed down to the capsule; but if the gland is found to be diseased, the tonsils together with their capsules are removed by the Sluder dull dissection method. He thinks that, when a substantial portion of one tonsil is diseased, with few exceptions both tonsils are diseased and require complete enucleation, but that only about 20 per cent. of all enlarged tonsils are diseased and require extracapsular enucleation.

Dr. Bryson Delavan[5] believes that the tonsil must have some useful function in nature which sometime will be better understood, and that the capsule is a valuable organ which should, if possible, be preserved for the protection and support of the pharyngeal wall and the prevention of cicatricial deformities after the operation. He thinks that such deformities are of common occurrence and are highly detrimental to

4. Layton, T. B.: Lancet, London, April 18, 1914.

5. Symposium before Brooklyn Pediatric Society, Oct. 28, 1914, New York Med. Jour., Dec. 5, 1914.

the future welfare of the patient. Not every large tonsil necessarily requires excision.

Henry L. Swain[5] says that the young, growing and healthy tonsils of children should not be confused with older adult tonsils which he characterizes as being of a retrograding, degenerating, and often diseased type of tissue. The common habit of always completely removing all faucial tonsils from all children whenever they come to operation, as for adenoids, and with no further excuse than that they may make trouble later on, is strongly condemned as being "unscientific, illogical and thoroughly reprehensible." He says that it would be quite as logical to remove all inflamed lymph-nodes from the neck, for the faucial tonsils are to all intents and purposes the exact counterpart of these nodes.

Hubert Arrowsmith[5] goes further than French and says that of those tonsils which need surgery at all before puberty, 90 per cent. may be satisfactorily dealt with by conservative measures, and only the remaining 10 per cent. may require complete tonsillectomy. He says that tonsillar disease may be induced by infection from other focal points, and that the tonsillar flora may be but surface contaminations and without clinical import. He has for many years favored conservatism in tonsillar surgery and is pleased that pediatrists and internists are gradually beginning to adopt the same view.

G. Hudson Makuen[5] describes some deformities that have followed tonsillar enucleations and how defects of voice and speech must necessarily follow such procedures. He also describes the so-called capsule of the tonsil, asserting that it is not, strictly speaking, a capsule at all but only that depressed portion of the pharyngobasilar aponeurosis in a recess of which the tonsil develops and to which it gradually becomes attached. This aponeurosis is composed of several layers of thin fascia, and in the young subject an extracapsular tonsillectomy may consist merely in the removal of the tonsil together with a very thin, single layer of fascia, which constitutes its so-called capsule; but in older subjects the layers of fascia have become so firmly united that it is impossible to separate them and a thorough enucleation of the tonsil may result in a kind of window resection of the pharyngobasilar aponeurosis down to the important muscles which it covers, leaving an extensive cavity to be filled in with granulation tissue. A tonsillectomy, therefore, in an adult is a much more extensive and difficult operation than it is in children.

NEW EXPERIMENTAL OBSERVATIONS ON THE FUNCTION OF THE TONSILS

In the course of a discussion of the numerous suggestions which have been put forth as to the functions of the tonsils, F. Henke[6] expresses his belief that there has been great exaggeration during recent years on the part of some writers in regard to the frequency with which the tonsils form the portal of entry for many general diseases for whose onset they have been held responsible. The great differences in the statistics of various writers, from 80 per cent. (Faerber), to 1.4 per cent. (Pibram), in the case of articular rheumatism, suggest that much doubt still exists on the matter, and it is still a question whether the acute tonsillitis sometimes observed in association with various diseases is not in reality a secondary localization of an infection which has gained an entrance by some other channel. In order to test the capacity of the tonsils for the absorption of particles from the food, a series of rabbits were fed for a week on food containing large quantities of soot and chinese ink. Subsequent microscopic examination never showed any trace of absorption of these substances by the tonsils, although they were freely taken up by the intestines. The results of Lexer, who fed rabbits on virulent streptococci, and after death of the animals found the organisms present in the tonsil-tissue, do not justify the conclusion which he draws, that the tonsils were the only, or even the chief portal of entry of the infective organisms. The latter were present also in other portions of the pharyngeal mucous membrane, and were in fact more numerous in the periphery of the tonsil, that is, in its capsule, and in the surrounding muscular and glandular tissue, than in the tonsil itself.

Somewhat in opposition to the view that even the normal tonsil is to be regarded as a weak spot through which infection commonly enters is the suggestion that it serves as a defensive mechanism, in virtue of the phagocytic action of the leukocytes which migrate actively to its surface. Brieger, however, showed that the cells which pass out of the tonsil-tissue are in reality lymphocytes, and was forced to postulate a lymph-stream which carried these cells passively to the surface. As Levenstein remarks, proof of such a lymph-stream has been hitherto wanting.

A very different view is that of Schoenemann, who regards the tonsils as submucous lymph-glands, and acute tonsillitis as due to infection reaching the tonsil from the area which it drains. Clinical experience lends much support to this idea, and its correctness has been established as a result of experimental injection of the nasal mucous

6. Henke, F.: Arch. f. Laryngol., 1914, xxviii, Part 2.

membrane carried out by Schoenemann in man, with iodin solution, and by Lenart and Henke in animals and man respectively, with solid particles in suspension. It may therefore be regarded as certain that in man there exists a direct lymphatic communication between the nose and the tonsils. A similar lymphatic communication was proved by Henke to exist between the mucous membrane covering the alveolus of the upper jaw and the tonsil, an observation which he claims to be new. As a result of numerous carefully conducted experiments, he was further able to satisfy himself that there exists a constant lymph current passing from the lining membrane both of the nose and of the gums towards the tonsils, and through it on to its free surface. Such a current must act as a powerful defensive mechanism against the entrance of micro-organisms, and the proof of its existence must dispose of the view that the tonsil is not only a useless organ, but a *locus minoris resistentiae*.

The function of the tonsils is therefore comparable to that of the ordinary lymphatic glands. They serve for the production of white blood corpuscles, and act as a filter for the lymph which passes through them. Foreign bodies, bacteria, etc., may be arrested in the tonsils as in the lymph-glands, and there rendered innocuous. As, however, the tonsils differ from the lymph-glands in having a large surface (much augmented by the presence of crypts) freely exposed in the pharynx, they offer an exceptional opportunity to the organism of freeing itself from foreign substances which have gained entrance to the lymph-stream.

It follows that tonsillitis, occurring either alone or in association with some other disease such as rheumatism or endocarditis, is seldom due to infective material gaining entry through the surface of the tonsil, but the result of a secondary infection conveyed by the lymph-stream, the portal of entry being in most cases somewhere in the nose, the accessory sinuses, or the mucous membrane of the mouth.

This view is in no way incompatible with the well-established fact that severe general infections do take their origin from diseases of the tonsil. In this connection it is necessary to distinguish carefully between healthy and diseased tonsils. When, as a result of marked pathologic changes, the tonsil has come to resemble, as Hopmann says, a "choked filter," it is obvious that it should be regarded as a constant source of danger to the body as a whole.

THE ETIOLOGIC RELATIONSHIP OF THE FAUCIAL TONSILS TO TUBERCULOUS CERVICAL ADENITIS IN CHILDREN

A. Philip Mitchell[7] states that in tuberculous disease of the upper deep cervical glands the faucial tonsils have an importance not hitherto

7. Mitchell, A. Philip: Jour. Laryngol., Rhinol. and Otol., April, 1914.

well enough recognized or understood. The position of the tonsils at the entrance to the digestive tract favors infection more with food than with inspired air, a fact of great consequence in considering the frequency with which cervical glands in children harbor the bovine type of tubercle bacillus. Further, the very direct and short pathway between the tonsils and the tonsillar lymphatic glands explains the frequency with which well-marked tuberculosis of these glands may be secondary to a small focus in a tonsil.

He has investigated the faucial tonsils from sixty-four consecutive cases of children suffering from tuberculous disease of the upper deep cervical glands; twenty-four (37.5 per cent.) of these cases showed histologic evidence of tuberculosis in the tonsils. There are no clinical signs by which the condition can be recognized. In the majority of cases the tonsil retains its normal appearance, is small and frequently receding. Occasionally the tonsil is flat and its surface fissured, or it may be hypertrophied, the external surface showing no ulceration. The chief sites for tuberculous lesions in the tonsil are: (1) surrounding the deeper parts of the crypts, especially the supratonsillar group; (2) immediately under the mucous membrane near the mouths of the crypts; (3) deep in the tonsil, close to the posterior capsule. The lesions may be localized or generalized. Experimental inoculation of guinea-pigs and rabbits with pieces of tonsillar tissue yielded positive results in nineteen cases (30 per cent.), and of these the bovine bacillus was present in twelve cases, and the human in three cases.

Mitchell has also investigated the hypertrophied faucial tonsils removed from ninety children, in whom the cervical glands showed no clinical evidence of tuberculous disease; six (6.5 per cent.) of these hypertrophied tonsils gave histologic evidence of tuberculous disease, while nine (10 per cent.) yielded positive results when inoculated into guinea-pigs. The bovine bacillus was present in three cases, and the human in one case.

In conclusion, he says, primary tuberculous disease of the faucial tonsils occurs much more frequently than previously recognized. Considering the frequency with which the upper deep cervical glands are infected secondarily to tuberculosis of the tonsils, there is absolute need of removal of the tonsils in all cases of tuberculous cervical adenitis. The hypertrophied faucial tonsil is the seat of primary tuberculosis rarely as compared with tonsils from cases of tuberculous cervical adenitis.

ASSOCIATION OF FOLLICULAR TONSILLITIS WITH ACUTE GASTRIC FEVER

Louis Fischer[8] says that follicular tonsillitis and acute gastric fever are seen in the infant, as well as in the older child, as a sequence to a deranged stomach, following overfeeding. Loss of appetite, or rather a refusal to eat, will be noted; all symptoms pointing to a gastric derangement will be present, and still the predominating symptom will be the patches or follicles on the tonsils, causing pain on swallowing. Fischer emphasizes that too much importance cannot be placed on the necessity for throat inspection in every child that refuses to eat.

The treatment he advocates is as follows: An alkaline laxative such as a 3- to 5-grain dose of compound jalap powder should be given and repeated every three hours until a thorough evacuation has been produced. During this eliminative treatment water should be given liberally, but no food. Locally for the throat, tincture of iodin diluted with an equal quantity of water should be applied once with the aid of a cotton swab. After the bowels have been thoroughly cleansed, chicken soup, skimmed milk or weak tea may be permitted. Afterward, one or two drops, depending on the age, of tincture of nux vomica may be given before meals.

FATAL CAVERNOUS SINUS THROMBOSIS FOLLOWING TONSILLITIS

H. J. Davis[9] reports the case of a healthy boy, aged 10, who developed on December 27 a unilateral parenchymatous tonsillitis. His two brothers had previously been laid up in the same house with follicular tonsillitis. This had run its usual course. On January 3 the temperature was 104 F., with rigors, and these continued in spite of all treatment until he died on January 13, the temperature being 107 F. January 5, antistreptococcic serum was injected, and the next day the palate and tonsil were incised. January 7, incision was made in the neck, but no pus was found. January 8, swab was taken from the wound and blood taken from elbow vein; swab was sterile, but after prolonged cultivation *Staphylococcus albus* was found in the blood. January 9, the diagnosis of cavernous sinus thrombosis was obvious. The eyelids were edematous and tightly closed over the eye, which was bulging; there was ecchymosis of the conjunctiva, and edema had spread to the forehead and face from blocking of the facial vein and extended down the neck. There was little to be seen in the throat except that the left tonsil was red and slightly enlarged. Incisions were made in the palate, face, neck and eyelids, and the conjunctiva was also incised and 5 minims of liq. ammon. fort. administered every

8. Fischer, Louis: Med. Rec., Nov. 21, 1914.
9. Davis, H. J.: Jour. Laryngol., Rhinol. and Otol., January, 1914.

two hours in water. January 10, twitchings and paresis of the leg supervened; lumbar puncture fluid clear; 4 c.c. drawn off apparently not under pressure. Fluid sterile and did not reduce Fehling's solution. Child died on January 13.

Davis believes that the infection of the cavernous sinus travelled through the facial vein, as it communicates by the angular vein with the ophthalmic vein in the orbit. The edema of the face was due to blocking of the facial vein.

KOPLIK'S SPOTS OCCURRING ON THE TONSILS OF A CHILD

Sydney R. Miller[10] reports the case of a child of 10 months who was suddenly seized with a laryngeal spasm, associated with a temperature of 104.5. Examination of the throat showed a dusky red mucosa with very large swollen tonsils on which were a number of small bluish, semitransparent, elevated bodies, less than pin-head size. These were diagnosed as Koplik's spots which, from a search of the literature, had never been seen in this location before.

The child recovered from the laryngeal spasm after being given a hot foot-bath and was relieved in every way. Within a short time the entire body was covered with a dusky red mottling, characteristic of measles.

Within two days after the appearance of the external rash, the tonsils subsided to normal and no spots could be seen.

Another interesting phenomenon in connection with this case was the discovery that the child was anaphylactic to egg-albumin, which gave rise to laryngeal stridor, fever to 103, an urticarial rash and a swelling of the tonsils. The symptoms came on within a half hour after feeding the child egg-white. A dilution of one drop of egg-albumin in a quart of water was tolerated. The strength was gradually increased until in about three months the child had become desensitized to such an extent that it can now be given one dram of pure egg-albumin without any trouble.

THE EPIPHARYNX IN CHILDREN

According to Edgar M. Holmes,[11] over 90 per cent. of all pathologic conditions met with in otology are due to some preexisting pathologic condition in the epipharynx or eustachian tube. He believes that by improved methods in treatment in this locality more and more ears can be saved. Many children affected with middle-ear disease may be entirely relieved by simply removing their adenoids, but it is also well known that many more are but temporarily relieved and then become as bad as before.

10. Miller, Sydney, R.: Bull. Johns Hopkins Hosp., March, 1914.
11. Holmes, Edgar M.: Ann. Otol., Rhinol. and Laryngol., March, 1914.

Were it not for cicatrices and their effect on the eustachian tube the subject of adenoids would be very simple. A large number of the children referred to the specialist by school inspectors do not need an operation and are far better off without one. If an operation has been done, these children should be seen and examined a few weeks afterward with especial reference to adhesions about the eustachian tubes. Holmes' nasopharyngoscope has been of great help in making a good satisfactory examination of the epipharynx.

The treatment is general and local. Gastro-intestinal conditions must be looked after; malnutrition and anemia, and each child's resistance should receive attention. Infections of the epipharynx are almost always associated with those of the nasal cavities. He advises against the douche and prefers medication by means of a dropper. A 10 to 20 per cent. solution of argyrol dropped through the nose has given satisfaction. The solution can be made to run into the ear or eustachian tube by properly tilting the head when held over a table in Rose's position. The removal of bands of adhesion about the eustachian tubes is done by means of special ring curets, the use of which requires some practice.

CICATRICIAL PHARYNGEAL DIAPHRAGM FOLLOWING SCARLET FEVER

J. F. O'Malley[12] reports the case of a boy, aged 5, who had scarlatina two years ago, and was then for about three months in a fever hospital. On returning from the hospital it was noticed that he "spoke through his nose," and the condition has become worse since then. He can swallow solids and liquids without difficulty, and there is no history of interference with breathing.

On examination of the throat one sees a diaphragm, appearing as a continuation downwards of the soft palate and formed by the union of the free edges of the two posterior pillars. It shuts off the nasopharynx from the oro- and hypopharynx and is complete except at the center of its upper and lower borders. The upper opening is a small space surrounding the normal uvula, in which the latter is free to move. At the lower border there are two openings, one on each side of a central adhesion, which passes obliquely downward and backward to the right and is attached to the posterior wall of the pharynx, opposite the level of the epiglottis. The anterior pillars, at their upper ends, blend with the new diaphragm, whilst the lower ends are normal and behind the latter. On the anterior aspect of the new formation the tonsils can be seen appearing rather superficial owing to the partial obliteration of the sinus tonsillaris.

12. O'Malley, J. F.: Jour. Laryngol., Rhinol. and Otol., August, 1914.

O'Malley describes the method of formation of these adhesions as follows: There was an intense inflammation with inflammatory infiltration, and at the same time a myositis which put the muscular tissue in a condition of paresis. The swelling and infiltration, especially in the young child, facilitated the coming together of the parts, and the intensity of the myositis prevented the mobility which would otherwise exist and enable the parts to come away from each other. A denudation of the epithelium proceeded at the same time, owing to the severity of the inflammation, and that facilitated the joining up.

TUMOR OF THE SOFT PALATE CONSISTING MAINLY OF SALIVARY GLAND TISSUE

Thomas Guthrie[13] reports the case of a boy, aged 8 years, with a pear-shaped tumor hanging from the right side of the soft palate. The tumor was covered with normal mucous membrane similar to that of the surrounding parts, and showed no signs of ulceration. When cut through the middle, after removal, the tumor measured 9 mm. longitudinally and 6 mm. transversely, and was found to consist of a mixed salivary gland of the submaxillary type. Guthrie had not been able to discover any record of a similar case.

DOUBLE ABDUCTOR PARALYSIS IN A CHILD, AGED EIGHT

C. W. M. Hope[14] reports the case of a child, aged 8, who was admitted to the hospital, 1913, with marked dyspnea. Up to fourteen days before admission was perfectly well; gradual onset of dyspnea, but voice was not noticed to be altered.

When first seen the voice was good, but there was marked dyspnea, sucking in of intercostal spaces and supra-clavicular regions; marked retraction of lower end of sternum, and slight cyanosis. Temperature was normal; pulse 120. On examination by the direct method under chloroform both cords were found fully adducted, normal in color, and no movement seen, either of them or of the arytenoids, which were of normal size. There was only a small area for aeration at posterior end of glottis. Intubation was tried with O'Dwyer's tubes, but they were coughed out within a few minutes of introduction. Tracheotomy was then performed. After four days tube was blocked by day and opened by night. Swab from larynx showed absence of Klebs-Loeffler bacilli.

Three weeks later cords showed some movement; there was slight abduction and also some movement of the arytenoids. Tracheotomy tube had been removed and left out on Jan. 14, 1914, but owing to night stridor was replaced (low tracheotomy) on Jan. 29, 1914. Skia-

13. Guthrie, Thomas: Jour. Laryngol., Rhinol. and Otol., February, 1914.
14. Hope, C. W. M.: Jour. Laryngol., Rhinol. and Otol., August, 1914.

gram of chest showed no enlargement of thymus gland or any increase in size of bronchial glands. The cause of the paralysis could not be determined.

SUSPENSION LARYNGOSCOPY IN CHILDREN

Albrecht[15] states that suspension laryngoscopy in children is much simpler than in adults. The reasons for this he ascribes partly to the upright position of the epiglottis, which often permits a satisfactory view as soon as the base of the tongue is pressed on, and partly to the slender build of the neck characteristic of childhood. He states that clinically the procedure has rendered more certain: (1) the removal of the larger infantile nodes ("screamer's nodes") analogous to the singer's nodes in adult life, and ascribed to habitual crying or screaming; (2) the operative treatment of laryngeal tuberculosis; (3) the operative treatment of papilloma, which he considers the great field, and of which he mentions nine cases thus treated. To these three procedures he adds a fourth, enucleation of the tonsils, stating that in operating under narcosis, and with the head dependent, suspension gives a good view of the tonsillar region, so that enucleation can be effected in a few minutes under the strictest visual control.

A CASE OF RECURRING LARYNGEAL POLYPI WITH TETANY

R. Bishop Canfield[16] reports the case of a child 2 years and 3 months old who had been growing more and more hoarse for six months prior to August, 1912, and for the past ten days had been showing a marked degree of dyspnea; cyanosis had been present for several hours, so that the respiration was gasping. A high tracheotomy was done and immediate relief obtained.

Nine months later the child was seen for the second time. He had been wearing the tube constantly and it had not been even removed for cleaning. The wound was in bad condition. Attempted removal brought on a brisk hemorrhage. This was stopped and two days later a bronchoscopic examination was made which revealed a mass of papillomatous tissue filling the larynx and extending down to the level of the lower end of the tracheotomy tube. This mass of tissue was removed and applications of absolute alcohol made; the tube was replaced. Two months later, the condition having not improved, a thyrotomy was performed and the growth thoroughly removed under ether. It was found to extend up onto the base of the tongue.

Ten days later the tracheotomy tube was removed, but had to be replaced and was worn for two months longer. At this time the larynx was intubated and the tube taken out of the trachea.

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15. Albrecht: Jour. Laryngol., Rhinol. and Otol., February, 1914.
16. Canfield, R. Bishop: Ann. Otol., Rhinol. and Laryngol., March, 1914.

Dec. 13, 1913, the intubation tube was removed under suspension laryngoscopy, but edema quickly came on because of relief of pressure and the tube was reinserted. The edema became so great, however, as to cover the top of the tube, and it was necessary to replace the tracheotomy tube again.

Five hours afterward the child complained of being cold and developed a tremor resembling a chill; the temperature rose to 103.8 F., respirations 28 to 40 and pulse 80. There was profuse sweating. Within two hours the tremor had developed into clonic convulsions, beginning in the face, then the arms, hands and fingers, and lastly the legs. The convulsions became almost continuous and lasted several hours; the child became stuporous; opisthotonus appeared; erythematous rash developed over the chest and face. Three days after the first tremor the convulsions became tetanic and from then on the case was plainly one of tetany. The attack lasted thirteen days, during which optic neuritis developed from edema and the child was blind. After this the child gradually improved, vision returned and is good, and the child still wears the tracheotomy tube.

The cause of the tetany was believed to be either a toxemia from ether or an injury to the parathyroid from hemorrhage during some of the operative manipulations.

SINUS SUPPURATION IN CHILDREN

Suppuration of the accessory sinuses is more common in children than is generally supposed and the following cases reported by Dan McKenzie[17] are very interesting.

Case 1.—Frontal sinusitis in a girl aged 7. There was a curious history in the case. About three months before she came to the hospital patient was overturned by a bicycle and thrown on her face. A fortnight later pain and swelling in the left supra-orbital region and around the left eye set in, together with headache and pyrexia. After about ten days of fever and headache, the patient being confined to bed, a sudden gush of pus from the left nostril took place. Thereupon the pain ceased, the fever left her, and the child was able to be up and about; but the discharge from the nose continued. When she came to the hospital pus was seen to be oozing freely from under the left middle turbinal. A skiagram showed well-marked frontal sinuses on both sides, and the left frontal sinus together with the left antrum threw shadows. Treatment was confined to nasal drainage; the left middle turbinal was removed and nasal antrotomy performed, and the discharge gradually ceased.

Case 2.—Double maxillary antrum suppuration in a girl, aged 12. After washing out the cavity several times with a Lichtwitz trocar, the radical antrum operation was performed on the left side and simple nasal antrotomy on the right. The discharge has now ceased.

Case 3.—Left frontal sinusitis in a girl aged 15; radical Killian operation; necrosis of the bridge. The patient is now aged 17, her operation having been performed two years ago. The case was one of ethmoidal suppuration with polypi. After curetting and drainage the presence of headache and local pain

17. McKenzie, Dan: Jour. Laryngol., Rhinol. and Otol., April, 1914.

led to the radical frontal sinus operation (Killian). The bridge necrosed and was removed a fortnight later, but the wound had healed with very little deformity on account of the natural flatness of the patient's nose. There was still a fair amount of discharge.

ORBITAL ABSCESS WITH OPTIC NEURITIS DUE TO ACUTE ETHMOIDITIS IN A CHILD

J. H. Guntzer[18] reports the case of a girl, aged 7 years, a normal child and in apparent good health, who came to the hospital on March 18, 1914. She had had no recent illness until the right eye became swollen two days before.

There was well-marked orbital cellulitis, the upper and lower lid swollen with tenderness over the inner margin of the orbit, marked exophthalmos with displacement of the eyeball downward and outward, ocular motion limited above and internally, the eye dilated outward. Diplopia; vision 20/200. Conjunctival blood vessels injected. Fundus examination showed the veins enlarged, tortuous, the arteries normal. Disk-color red; margin blurred. Diagnosis: Optic neuritis.

The orbital abscess was incised at the most prominent portion on the nasal side below the brow in order to relieve the ocular pressure. The following day the ethmoidal labyrinth was exenterated by the external route. The patient made an uninterrupted recovery. Six weeks after operation the eye-ground had entirely cleared up with vision 20/20.

1517 Walnut Street.

18. Guntzer, J. H.: Laryngoscope, September, 1914.

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